Hepatitis A vaccination in adults - temporary recommendations

July 2018 update
About Public Health England

Public Health England exists to protect and improve the nation’s health and wellbeing, and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

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Hepatitis A vaccination temporary recommendations

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Summary of changes to document:
- the hepatitis A adult vaccine options were amended in view of improving monovalent hepatitis A vaccine supplies and discontinuation of some combination hepatitis A /typhoid vaccines
- the advice table for MSM vaccine options was removed as vaccine for GUM and HIV clinics that was procured in response to the outbreak is still available
Hepatitis A vaccine recommendations and advice for pre and post exposure immunisation and boosting in adults

Hepatitis A immunisation recommendations have been updated in light of the ongoing hepatitis A outbreak primarily affecting men who have sex with men (MSM) and the shortage of global hepatitis A vaccine that has severely impacted UK supply. These recommendations include updated travel vaccine recommendations and temporary advice where the availability of monovalent hepatitis A vaccine is limited. Supplies are improving and are expected to improve further throughout 2018. As a result recommendations have been modified in June 2018 to encourage the use of adult antigen rather than paediatric antigen content vaccines in adults where possible. However, as the UK’s full vaccine allocation will not be available from all manufacturers, the market is likely to remain constrained and these recommendations offer alternatives when the availability of monovalent adult hepatitis A vaccine is limited.

1.1 Vaccine recommendations

Hepatitis A vaccine is highly effective in preventing infection if given prior to exposure.

PHE recommends that all MSM attending GUM and HIV clinics without reliable evidence of previous vaccination or infection should be opportunistically offered hepatitis A vaccination. Hepatitis A vaccines (Havrix, Vaqta or Avaxim) that were centrally procured in response to the outbreak in MSM continue to be available to GUM and HIV clinics through ordering via ImmForm. This stock can be used for both the priming dose and the subsequent boosting dose given at least 12 months after the first dose.

NaTHNaC has updated its hepatitis A immunisation recommendations. As a result, hepatitis A vaccination will no longer be recommended for most travellers visiting a number of countries. Please visit the NaTHNaC website for a full list of countries for which hepatitis A vaccine is recommended prior to travel.

Hepatitis A is also recommended as post exposure treatment within 14 days of exposure to a person with hepatitis A, or during outbreaks. See the Public Health Control and Management of Hepatitis A guidance for further details. Note that post exposure vaccination should not be delayed and vaccine should be prioritised for these individuals.
1.2 Vaccine options

Alternative vaccine options have been formulated in response to shortages of adult hepatitis A vaccine, following a review of immunogenicity data, and have been agreed by the Joint Committee for Vaccination and Immunisation (JCVI) in June 2017. PHE has converted those options into temporary advice to offer alternatives when the availability of monovalent hepatitis A vaccine is limited the advice is based on a broad assessment considering the following criteria:

- risk of acquiring infection
- risk of complications of infection
- immune response to vaccine products of varying antigen content
- vaccine availability and number of doses required
- compliance with vaccine schedule
- feasibility of delivery in settings
- likelihood of individual already being immune

The advice provided is not absolute; it requires some clinical judgement and hence is not presented in an algorithm, but in tables. The advice will be updated as vaccine availability changes.

The tables below include advice for pre-exposure vaccination of people travelling abroad, for post exposure prophylaxis and for boosting primed adult patients. Note that post exposure vaccination should not be delayed and vaccine should be prioritised for these individuals.

Some of these vaccine options will be off-label use of licensed products. For further information on off-label use of vaccines see: https://www.gov.uk/government/publications/off-label-vaccine-leaflets

1.3 Advice tables

Table 1: Antigen content of hepatitis A containing vaccines available in the UK
Table 2: Pre-exposure dose-sparing options for hepatitis A vaccination in adults travelling overseas to preserve adult monovalent stock for groups most likely to benefit
Table 3: Post-exposure dose-sparing options for hepatitis A vaccination to preserve adult monovalent stock for groups most likely to benefit
Table 4: Vaccine options for boosting primed patients
### Table 1 Antigen content of hepatitis A containing vaccines available in the UK

<table>
<thead>
<tr>
<th>HepA Vaccine formulation</th>
<th>Trade name</th>
<th>HepA vaccine antigen content</th>
<th>Adult dose hepA antigen equivalent</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADULT MONOVALENT HEPA</td>
<td>AVAXIM</td>
<td>160 U</td>
<td>Full dose</td>
<td>Sanofi Pasteur (SP)</td>
</tr>
<tr>
<td></td>
<td>HAVRIX</td>
<td>1440 EU</td>
<td>Full dose</td>
<td>GlaxoSmithKline (GSK)</td>
</tr>
<tr>
<td></td>
<td>VAQTA</td>
<td>50 U</td>
<td>Full dose</td>
<td>Merck Sharp &amp; Dohme Limited (MSD)</td>
</tr>
<tr>
<td>PAEDIATRIC MONOVALENT HEPA</td>
<td>HAVRIX</td>
<td>720 EU</td>
<td>Half-dose</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td>VAQTA</td>
<td>25 U</td>
<td>Half-dose</td>
<td>MSD</td>
</tr>
<tr>
<td>ADULT COMBINATION HEPATITIS A/B</td>
<td>TWINRIX</td>
<td>720 U</td>
<td>Half-dose</td>
<td>GSK</td>
</tr>
<tr>
<td>PAEDIATRIC COMBINATION HEPA/HEPB</td>
<td>TWINRIX</td>
<td>360 U</td>
<td>Quarter-dose</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td>AMBIRIX</td>
<td>720 EU</td>
<td>Half-dose</td>
<td>GSK</td>
</tr>
</tbody>
</table>

### Table 2 Pre-exposure dose-sparing options for hepatitis A vaccination in people travelling overseas to preserve adult monovalent stock for groups most likely to benefit

<table>
<thead>
<tr>
<th>Travellers to high risk countries</th>
<th>Order of preference</th>
<th>Immunocompetent adults under 60 years (including HIV+ with CD4 count ≥ 500 cells/mm³)</th>
<th>Immunocompromised adults of any age Including HIV+ with CD4 count&lt;500 cells/mm³</th>
<th>Adults of any age with chronic liver disease</th>
<th>Aged 60 years or over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower and short term risk in areas of poor sanitation Note: it is important that vaccine is given at least 4 weeks prior to travelling, particularly for individuals who are HIV positive, have chronic liver disease or are over 60 years old, to allow sufficient time for an immune response</td>
<td>1st</td>
<td>Single dose of adult monovalent hepatitis A vaccine</td>
<td>Single dose of adult monovalent hepatitis A vaccine</td>
<td>Single dose of adult monovalent hepatitis A vaccine</td>
<td>Single dose of adult monovalent hepatitis A vaccine</td>
</tr>
<tr>
<td></td>
<td>2nd</td>
<td>Single dose of adult combination HepA/HepB vaccine</td>
<td>Two simultaneous doses of adult combination HepA/HepB vaccine</td>
<td>Single dose of adult combination HepA/HepB vaccine</td>
<td>Single dose of adult combination HepA/HepB vaccine</td>
</tr>
<tr>
<td></td>
<td>3rd</td>
<td>Single dose of paediatric monovalent HepA vaccine</td>
<td>Two simultaneous doses of paediatric monovalent HepA vaccine (unless also requiring hepatitis B)</td>
<td>Single dose of paediatric monovalent HepA vaccine* (unless also requiring hepatitis B)</td>
<td>Single dose of paediatric monovalent HepA vaccine*</td>
</tr>
</tbody>
</table>

**Rationale and considerations**

- A single dose of vaccines containing half (720EU/25U) the adult hepatitis A antigen content has equivalent immunogenicity at one month to vaccines containing twice the antigen content in immunocompetent younger adults.
- Those who are immunocompromised, have chronic liver disease or aged over 60 years have a lower and slower response to vaccine.
- Those with chronic liver disease and those aged over 60 years are also at higher risk of the complications of hepatitis A infection; however among travellers, there is more time to respond.
- Combination HepA/HepB vaccine may be preferred if Hep B vaccination is also indicated for travel.
- Simultaneous doses (at same site) are preferred to separate doses for improved compliance.
- Other measures such as careful attention to food and water hygiene and scrupulous hand washing are particularly important in travellers who have chronic liver disease and aged over 60 years.

*If the travel is assessed to be very high risk and there is concern that hygiene measures cannot be followed, then two simultaneous doses of paediatric /adult combination vaccine could be considered.
## Table 3 Post-exposure options for hepatitis A vaccination

<table>
<thead>
<tr>
<th>Post exposure vaccination of susceptible contacts of cases</th>
<th>Order of preference</th>
<th>Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Order of preference</td>
<td>Immunocompetent adults under 60 years (including HIV positive with CD4 count ≥ 500 cells/mm³)</td>
</tr>
<tr>
<td></td>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Single dose of adult monovalent HepA vaccine</td>
</tr>
<tr>
<td></td>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>Single dose of paediatric monovalent HepA vaccine</td>
</tr>
<tr>
<td></td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>Single dose of adult combination HepA/HepB vaccine</td>
</tr>
</tbody>
</table>

### Rationale and considerations
- A single dose of vaccines containing half (720 EU/ 25 U) the adult hepatitis A antigen content has equivalent immunogenicity at one month to vaccines containing twice the antigen content in immunocompetent younger adults; however there is a lack of data and experience on post exposure use of half-adult antigen content in adults.
- Those who are immunocompromised, have chronic liver disease or aged over 60 years have a lower and slower response to vaccine.
- Those with chronic liver disease and those aged over 60 years are also at higher risk of the complications of hepatitis A infection.
- Two simultaneous doses of combination hepatitis A/B vaccine may be preferred to two simultaneous doses of paediatric vaccine in immunocompromised persons who are HIV positive as they may also have poorer response to hepatitis B vaccine so additional hepatitis B dose may improve their hepatitis B response.
- Simultaneous doses are preferred to separate doses for improved compliance.
- People over 60 years may already be immune to Hepatitis A (HAV IgG positive) so testing should be considered prior to providing HNIG if feasible to avoid unnecessary administration of a blood product which carries theoretical risks of transmission of unidentified infectious agents; testing should not delay post-exposure vaccine.
### Hepatitis A vaccination temporary recommendations

#### Table 4 Vaccine options for boosting primed patients

<table>
<thead>
<tr>
<th>Adult antigen content of priming dose</th>
<th>Full-dose hepatitis A antigen (1440 EU / 50U)</th>
<th>Half-dose hepatitis A antigen (720 EU / 25U)</th>
</tr>
</thead>
</table>
| **HepA containing vaccines that could have been given as priming dose** | Adult monovalent HepA vaccine
Combination hepatitis A /typhoid vaccine
Two doses of paediatric monovalent HepA vaccine
Two doses of adult combination HepA/HepB vaccine | Single dose of combination hepatitis A/B vaccine (Twinrix Adult or Ambrix)
Single dose of paediatric monovalent HepA vaccine |
| **Recommendations for boosting in immunocompetent individuals (including HIV positive with CD4 cell count ≥500 cells/mm³)** | Single dose of adult monovalent HepA vaccine at 5 years
OR
Single dose of paediatric monovalent HepA vaccine at 5 years
OR
Single dose of adult combination HepA/HepB vaccine at 5 years | Single dose of adult monovalent HepA vaccine at 1 year
OR
Single dose of paediatric monovalent HepA vaccine at 1 year
OR
Single dose of adult combination HepA/HepB vaccine at 1 year |
| **Recommendations for boosting immunocompromised individuals including those HIV positive with CD4 cell count <500 cells/mm³), persons with chronic liver disease, and those over 60 years old** | Single dose of adult monovalent HepA vaccine at 5 years
OR
Single dose of paediatric monovalent at 5 years
OR
Single dose of combination HepA/HepB vaccine at 5 years | Single dose of adult monovalent HepA vaccine at 1 year
OR
Two consecutive paediatric monovalent HepA vaccine doses at 1 year at least 4 months apart
OR
Two consecutive adult combination HepA/HepB vaccine doses at 1 year at least 4 months apart |

#### Rationale / considerations for choice of boosting dose

- Boosting can be delayed for up to 5 years in most situations. For individuals at ongoing risk of Hepatitis A exposure and for MSM, boosting should be given 6-12 months after the first dose.
- If an adult is primed with half dose antigen content vaccine, waning may occur sooner.
- If priming has been effective, boosting does not require a large amount of antigen: in an immunocompetent person primed with full-dose antigen content vaccine, half-dose antigen content vaccine is likely to provide adequate boosting.
- In those in whom priming may not have been optimal, e.g. immunocompromised HIV positive individuals, those with chronic liver disease, and persons over 60 years who received half dose antigen content, a further prime before boost (prime-prime-boost) is recommended with an interval of at least 4 months between doses.
- If at continuing risk of hepatitis B, further doses of hepatitis B containing vaccine should be given according to the recommended schedule (see chapter 18, The Green Book: Immunisation against Infectious Disease
- If at continuing risk of typhoid, further doses of inactivated typhoid containing vaccine should be given according to the recommended schedule (see chapter 23, The Green Book: Immunisation against Infectious Disease
Other resources


Immunoglobulin handbook for hepatitis A: https://www.gov.uk/government/publications/immunoglobulin-when-to-use

NaTHNaC: list of countries for which hepatitis A vaccine is recommended prior to travel: https://travelhealthpro.org.uk/countries