Hepatitis B vaccine recommendations during supply constraints

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Outline of the presentation

• UK context: hepatitis B vaccination
• Alert and escalation
• Response and risk mitigations
  • Guidance: temporary recommendations
  • Controlled central stock management
  • Communications and publications
• Impact of countermeasures
• Recovery plan
• Challenges
Hepatitis B vaccination in the UK

- Selective and universal immunisation policy
  - Routine infant immunisation since 2017
  - Selective immunisation since 1990s: neonatal, adult risk groups

- Vaccine procurement – no national tender
  - Monovalent HepB and bivalent Hep A/HepB: non-centrally procured vaccine; purchased by providers directly from manufacturers (GSK and MSD) or wholesalers
  - Infanrix-hexa (DTaP/IPV/Hib/HepB): centrally procured for national programme

- Providers = NHS and non-NHS organisations:
  - NHS Trusts (acute and mental health hospitals, ambulance trusts), retail pharmacies, General Practice, travel clinics, occupational health services, private hospitals and clinics, sexual health clinics, community drug and alcohol services, prison services

- Commissioners “contract” providers to deliver services such as vaccination
  - Primary care (GP): Clinical Commissioning Groups
  - Sexual health, community drug services: Local Government
  - NHS secondary care services: NHSE
Broad indications for hepatitis B vaccination

- **Green Book: Immunisation against infectious disease**
- Post exposure vaccination
  - Babies born to hepatitis B infected mothers
  - Significant exposures (e.g. community needle-stick injury)
- Pre exposure vaccination: behavioural, clinical, and occupational risk groups
  - MSM, people who inject drugs, prisoners, foster parents, travellers, household contacts
  - Patients with renal insufficiency, people with chronic liver disease
  - Health and social care staff – including laboratory workers and ancillary staff
  - Non-health first responders (police, fire, mountain rescue), custodial (prison guards)
Alert and escalation

- May-June 2017: Notification from manufacturers that UK supplies will be affected by manufacturing issue
  - some stock restrictions implemented
- June 2017: PHE issues warning and initial advice in e-bulletin *Vaccine Update*
- July 2017: PHE notified that situation will become critical
  - Usual demand ~150k adult doses and 10k paediatric doses per month
  - 1/3 of usual GSK stock available over August and MSD will be out of stock
- July 24 – Aug 7: PHE develops temporary guidance and communications
- 4 August 2017: PHE National Enhanced Incident declared; CMO alerted
- PHE National Incident Management Team (IMT) established
  - Strategic aims: to prioritize vaccine supply to those at highest immediate risk and preserve scarce stock during the period of constraint for these individuals
  - Strategic and operational response agreed to mitigate risks
  - De-escalation when assurance of sufficient supply to meet current and future demand
  - Official letters from PHE and DH to manufacturers
Response – reduce demand

- PHE Guidance
  - Temporary recommendations (Aug 2017)
  - Advice for people whose vaccination has been deferred (Aug 2017)
  - Use of combination vaccine for travellers (Nov 2017)
  - Recovery plan for phased re-introduction of vaccine as supplies improve (Feb 2017)
  - NaTHNaC: travel health advice

- Scientific “sign off” and endorsement
  - DH sponsored independent expert committee: Joint Committee on Vaccination and Immunisation (NITAG)
  - Chief Medical Officer
  - NHSE Hepatitis clinical lead

- Managed central stock control
  - Forecasting based on estimated demand and need
  - PHE /DH /manufacturer agreed vaccine ordering restrictions

- Communications
Temporary recommendations – key principles

• Prioritise scarce supply for those at highest IMMEDIATE risk
• Provide advice to individuals whose vaccination is deferred and flag them for recall
• Advise other ways of avoiding exposure to hepatitis B
• Use alternative vaccines and presentations (e.g. vials vs PFS) where appropriate
• Use dose sparing schedules and defer routine boosters
• Order and manage stock responsibly
  • Liaise with clinical leads (across departments in Trusts)
  • Estimate stock required for highest risk groups
  • Order small amounts frequently
  • Avoid stockpiling
### Risk based prioritisation

<table>
<thead>
<tr>
<th>Prioritisation</th>
<th>Exposure type</th>
<th>Examples of individuals in this category (not exhaustive but for illustration only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Highest risk and urgency</td>
<td>Post exposure</td>
<td>Substantial exposure to infected blood from a known hepatitis B infected source</td>
</tr>
<tr>
<td>2</td>
<td>Post exposure</td>
<td>Other exposure to a known hepatitis B infected source</td>
</tr>
<tr>
<td>3</td>
<td>Post exposure</td>
<td>Exposure to an unknown source</td>
</tr>
<tr>
<td>3</td>
<td>Pre-exposure</td>
<td>Priming for unavoidable, high and imminent risk</td>
</tr>
<tr>
<td>3</td>
<td>Pre-exposure</td>
<td>Priming for unavoidable, high and imminent risk, with high risk of onward transmission and co-circulating viruses e.g. HIV, HDV</td>
</tr>
<tr>
<td>4</td>
<td>Pre-exposure</td>
<td>Priming for those at lower risk and those that can access advice in the event of a recognised exposure</td>
</tr>
<tr>
<td>4</td>
<td>Pre-exposure</td>
<td>Priming for those at lower risk or where risk may be avoided or delayed</td>
</tr>
<tr>
<td>5 Lowest risk and urgency</td>
<td>Pre-exposure</td>
<td>Boosting and reinforcing doses</td>
</tr>
</tbody>
</table>
### Vaccine choice for post exposure

<table>
<thead>
<tr>
<th>Post-exposure vaccination</th>
<th>Order of preference</th>
<th>Infants born to hepatitis B infected mothers</th>
<th>Other children exposed to a known or unknown source of hepatitis B</th>
<th>Adults exposed to a known or unknown source of hepatitis B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full risk assessment needed: hepatitis B status of source, significance of exposure, vaccination status of recipient as per Green Book and immunoglobulin handbook</td>
<td>1st</td>
<td>Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
<td>Paediatric combination HepA/B vaccine (Twinrix paediatric)</td>
<td>Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
</tr>
<tr>
<td></td>
<td>2nd</td>
<td>Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
<td>High dose paediatric HepA/B vaccine (Ambirix)</td>
<td>Adult combination HepA/B vaccine (Twinrix)</td>
</tr>
<tr>
<td></td>
<td>3rd</td>
<td>Paediatric combination HepA/B vaccine (Twinrix paediatric)</td>
<td>Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
<td>High dose paediatric HepA/B vaccine (Ambirix)</td>
</tr>
<tr>
<td></td>
<td>4th</td>
<td>High dose paediatric or adult combination HepA/HepB vaccine (Ambirix or Twinrix)</td>
<td>Adult monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
<td>Two simultaneous doses of paediatric combination HepA/B vaccine (Twinrix Paediatric)</td>
</tr>
<tr>
<td></td>
<td>5th</td>
<td>Combination DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
<td>Adult combination HepA/HepB vaccine (Twinrix)</td>
<td>Renal HepB vaccine (Fendrix or HBVaxPRO40)</td>
</tr>
</tbody>
</table>

Urgent testing of the source should be done if their hepatitis B status if unknown.

Give HBIG where indicated (but do not substitute vaccine with HBIG)
Special considerations for infants born to hepatitis B infected mothers

- About 3000 babies born each year - identified via universal antenatal screening programme
- No delay in birth dose of vaccine for infants born to hepatitis B infected mothers
- Paediatric monovalent HepB vaccine should be prioritised for the birth dose
- Combination DTP/IPV/Hib/HepB is licensed from 6 weeks of age and may be used for second and subsequent doses.
- In infants who have received the birth dose on time and where monovalent hepatitis B is not available, the second dose may be delayed to six weeks of age and given as DTaP/IPV/Hib/HepB, with further doses given promptly at 12 and 16 weeks of age.
- Boosting at 12 months and/or pre-school can be deferred, although the recommended test for HBsAg at 12 months of age should be done on time.
# Vaccine choice for pre exposure

<table>
<thead>
<tr>
<th>Order of preference</th>
<th>Children</th>
<th>Immunocompetent adults</th>
<th>Adults with immunosuppression</th>
<th>Adults of any age with renal failure who are pre-dialysis or on dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>Paediatric combination HepA/B vaccine (Twinrix paediatric)</td>
<td>Adult monovalent HepB vaccine (unless requiring hepatitis A)</td>
<td>Renal HepB vaccine (Fendrix or HBVaxPRO40)</td>
<td>Renal HepB vaccine (Fendrix or HBVaxPRO40)</td>
</tr>
<tr>
<td>2nd</td>
<td>Paediatric monovalent HepB vaccine (EngerixB or HBVaxPRO)</td>
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Dose sparing schedules and boosting

<table>
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<tr>
<th>Dose sparing option</th>
<th>Rationale</th>
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<tr>
<td><strong>Schedule options for pre-exposure primary immunisation</strong></td>
<td></td>
</tr>
</tbody>
</table>
| Avoid using 0, 7, 21 day (super-accelerated) schedule - preferentially use standard (0, 1, 6 months) or, if rapid protection required, the accelerated schedule (0, 1, 2 months) | • The super-accelerated schedule is wasteful in the current supply climate. Because the immune response following 3 doses with the super accelerated schedule is lower than that with the standard or accelerated schedules, deferral of the reinforcing/booster dose at 12 months is more risky
• For most indications, particularly travel and occupational health, there should be sufficient time to use the standard or accelerated course
• Limited data suggest that, in healthy adults over 18 years, two doses at 0 and 1 months will provide equivalent protection to 3 doses at the super-accelerated schedule |
| Defer third dose of primary pre-exposure immunisation to at least 6 months in those not at immediate risk of exposure who can recognise exposure and access care promptly | • Equivalent protection achieved after 3 doses with 0,1, 6 month and 0,1,2 month schedules
• In healthy adults and children, a high proportion will have started to respond after a second dose of hepatitis B vaccine and a completing dose given after an exposure should provide rapid protection. |
| **Boosting deferral** |
| In immunocompetent individuals who have completed a primary immunisation course at 0, 1, 2 months | • Although knowledge about the duration of protection against infection and disease is still incomplete, studies demonstrate that, among successfully vaccinated immunocompetent individuals, protection against chronic infection persists for 20-30 years or more. |
| In immunocompetent healthcare and lab workers, who have completed a primary immunisation course, defer the single booster dose currently recommended for five years after the primary course for at least another 12 months | • WHO have concluded that there is no compelling evidence for recommending a booster dose of hepatitis B vaccine in routine immunisation programmes. |

BOOSTER DOSES NO LONGER RECOMMENDED – JCVI ADVICE, FEB 2018
Controlled central stock management

- PHE estimated vaccine demand from priority groups 1-3 based on NHS and company sales data
- Manufacturers agreed to release vaccine only for priority groups 1-3
- DH and PHE worked with manufacturers to set monthly maximum ordering quantities (MOQs) set to meet estimated demand and prevent stockpiling
  - Allocation based on an assessment of the proportion of vaccines used by those customers for individuals in the highest priority groups 1-3
  - Some providers e.g. NHS Trusts got larger allocations (for A&E PEP, sexual health clinics and staff undertaking EPP) than other customers e.g. GPs, retail pharmacies, universities could not order a stock of adult vaccine
- Override mechanism established for additional doses / volume above MOQ if justification / verification given
- **At-risk infants**: rapid stocktake of birth dose availability in maternity units; Infanrix hexa ordering opened early
- PHE / DH situation weekly monitoring calls with GSK and MSD
### Communications and publications

<table>
<thead>
<tr>
<th>News item on NaTHNaC website</th>
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<tbody>
<tr>
<td>Letter to Dentists</td>
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<tr>
<td>Letter to NHS OH Departments</td>
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<tr>
<td>Letter to GPs</td>
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<tr>
<td>Letter to NHS Medical Directors (includes implications for A&amp;E Departments)</td>
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<tr>
<td>Letter to University Deans</td>
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<tr>
<td>BHIVA / BASHH advice</td>
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<tr>
<td>Letter for NHS111</td>
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<tr>
<td>CAS Alert</td>
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<tr>
<td>Letter to nurses</td>
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<tr>
<td>Letter to community pharmacists</td>
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<tr>
<td>Memo to BVHG/BGS/BASL members</td>
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<tr>
<td>Drug and Drinks News item</td>
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<td>Email to liver charities</td>
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<tr>
<td>Post on Royal College of Emergency Medicine website</td>
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<tr>
<td>Email to NHS Trust pharmacists</td>
</tr>
<tr>
<td>Letter to NHS Screening and Immunisation Leads and GPs regarding early opening of hexavalent vaccine ordering for babies born to hepatitis B infected mothers</td>
</tr>
</tbody>
</table>

### Plan for phased re-introduction of hepatitis B vaccine for lower priority groups 2018

Ref: Gateway number: 2017808  
PDF, 247KB, 8 pages  
This file may not be suitable for users of assistive technology. [Request an accessible format](#).

### Hepatitis B: vaccine recommendations during supply constraints

Ref: PHE gateway number 2017256  
PDF, 221KB, 17 pages  
This file may not be suitable for users of assistive technology. [Request an accessible format](#).

### Temporary Addendum: Combined hepatitis A and B vaccine use in travellers

Ref: PHE publications gateway number 2017585  
PDF, 139KB, 1 page  
This file may not be suitable for users of assistive technology. [Request an accessible format](#).

### What to do if you have to wait for a dose of hepatitis B vaccine: advice for patients

Ref: PHE publications gateway number 2017260  
PDF, 159KB, 4 pages  
This file may not be suitable for users of assistive technology. [Request an accessible format](#).
Communications and publications
Challenges - legal & regulatory

- Competition laws prevent release and sharing of stock status between manufacturers or by PHE and other manufacturers
- Manufacturers cannot refer customers to off-label use of alternative vaccine products; they can signpost customers to the PHE temporary guidance
- Only licensed products in UK are from GSK and MSD; UK providers cannot use unlicensed vaccines if they have any licenced stock available
- Legal restrictions in moving vaccine stock between clinical entities
Challenges - strategic

- Stock control: no central procurement, stockpile or supply of hepatitis B vaccine so PHE/DH have no direct control over stock usage
  - No routine stocktake in providers
- Limited manufacturer visibility of supply and reduced allocations – difficult to forecast
- Lack of clarity of clinical responsibility and leadership for non-centrally procured vaccine issues in NHS and DH
- Multiple commissioners, providers, and clinical specialties implicated
  - No single, effective communication channel
- Large uncertainty around estimated numbers of patients/staff in each group where vaccination indicated
  - Dependent on sales and reimbursement data which likely reflects demand rather than actual need (e.g. excessive travel use)
Challenges - operational

- Interpretation of guidance as “absolute” “blanket” recommendations
  - Reluctance to undertake individual risk assessment
- Perceived potential for increased pressures on emergency and urgent care services
- Patients being bounced between services as lack of any prior formal agreement on responsibility for vaccination of these groups
  - Vaccine shortage used as an excuse not to vaccinate
- Concern that some services simply stopped vaccinating e.g. community drug services – issues:
  - Higher cost of alternative products and not contracted to provide them
  - Person ordering vaccine different to person immunising
  - No directive in place to allow nurse administration of alternative product
- Parallel market operating in retail pharmacies and private travel clinics can undermine prioritisation
- Concomitant shortage of hepatitis A vaccine and HAV outbreak in MSM
Thank you

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Resources

• Hepatitis B vaccine recommendations during supply constraints https://www.gov.uk/government/publications/hepatitis-b-vaccine-recommendations-during-supply-constraints

• Immunisation against Infections Disease (the Green Book) Department of Health (2006). Hepatitis B Chapter 18


• The National Travel Health Network and Centre (NaTHNaC) http://nathnac.net/#/

• Information on off-label use of vaccines https://www.gov.uk/government/publications/off-label-vaccine-leaflets