Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Comvax; ***Austria:*** Procomvax; ***Cz.:*** Procomvax; ***Ger.:*** Procomvax†; ***Gr.:*** Procomvax; ***Ital.:*** Procomvax; ***Mex.:*** Comvax; ***Neth.:*** Procomvax; ***NZ:*** Comvax; ***Pol.:*** Procomvax; ***Port.:*** Procomvax; ***USA:*** Comvax.

Haemophilus Influenzae and Meningococcal Vaccines

Profile

A combined Haemophilus influenza type b and meningococcal C conjugate vaccine is available for active immunisation in some countries; in the UK a single dose may be given to children between 1 and 10 years of age who have completed a primary vaccination course of diphtheria, tetanus, pertussis, and polio. Two doses given 2 months apart may be given to asplenic children (over 10 years of age) or adults who have not been previously immunised.

Preparations

Proprietary Preparations (details are given in Part 3)
UK: Menitorix.

Haemophilus Influenzae and Poliomyelitis Vaccines

ATC — J07CA04.

Profile

Combined haemophilus influenzae type b conjugate and inactivated poliomyelitis vaccines have been used in some countries for active immunisation of infants.

Preparations

Proprietary Preparations (details are given in Part 3)
Norw.: Act-HIB Polio†; ***Swed.:*** PolioHib†.

Haemorrhagic Fever with Renal Syndrome Vaccines

HFRS Vaccine; Vaccinum Haemorrhagia Febris cum Renis Sindronum; Vacunas de la fiebre renal epidémica.

Description. A fluid or freeze-dried preparation of a suitable hantavirus grown in the neural tissue of suckling rodents or in cell cultures and inactivated. The fluid vaccine should be stored at 2° to 8° and not allowed to freeze. The freeze-dried form should be stored below 10°.

Profile

Inactivated viral vaccines against haemorrhagic fever with renal syndrome have been investigated and are available in some countries, but there have been problems producing a sufficient and sustained immune response.

◊ References.

1. Sohn YM, *et al.* Primary humoral immune responses to formalin inactivated hemorrhagic fever with renal syndrome vaccine (Hantavax): consideration of active immunization in South Korea. *Yonsei Med J* 2001; **42:** 278–84.
2. Cho HW, *et al.* Review of an inactivated vaccine against hantaviruses. *Intervirology* 2002; **45:** 328–33.
3. Park K, *et al.* Protective effectiveness of hantavirus vaccine. *Emerg Infect Dis* 2004; **10:** 2218–20.

Helicobacter Pylori Vaccines

Vacunas de Helicobacter pylori.

Profile

Vaccines against *Helicobacter pylori* are being developed for prophylaxis of peptic ulcer disease and gastric cancer.

◊ Studies in *animals* have shown the feasibility of both prophylactic and therapeutic vaccination against *Helicobacter pylori* infection, but there have been few studies in humans. Encouraging results have been obtained with parenteral, multicomponent, aluminium hydroxide-based vaccines in terms of safety and immunogenicity. In contrast, preliminary results obtained with mucosally delivered single-component vaccines have been disappointing, partly due to the intrinsic difficulty in developing purified proteins that are sufficiently immunogenic following mucosal delivery. Studies are ongoing into the mechanisms by which the host's genetic make-up modifies the inflammatory and immunological response to *H. pylori*.[1-4]

1. Ruggiero P, *et al.* The quest for a vaccine against Helicobacter pylori: how to move from mouse to man? *Microbes Infect* 2003; **5:** 749–56.
2. Sutton P, Doidge C. Helicobacter pylori vaccines spiral into the new millennium. *Dig Liver Dis* 2003; **35:** 675–87.
3. Del Giudice G, Michetti P. Inflammation, immunity and vaccines for Helicobacter pylori. *Helicobacter* 2004; **9** (suppl 1): 23–8.
4. Agarwal K, Agarwal S. Helicobacter pylori vaccine: from past to future. *Mayo Clin Proc* 2008; **83:** 169–75.

Hepatitis A Immunoglobulins

Inmunoglobulinas contra la hepatitis A.

ATC — J06BB11.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.

Ph. Eur. 6.2 (Human Hepatitis A Immunoglobulin; Immunoglobulinum Humanum Hepatitidis A). A liquid or freeze-dried preparation containing human immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from selected donors having specific antibodies against the hepatitis A virus. Normal immunoglobulin may be added. It contains not less than 600 international units/mL. The liquid preparation should be stored, protected from light, in a sealed, colourless, glass container. The freeze-dried preparation should be stored, protected from light, in a colourless, glass container under vacuum or under an inert gas.

Profile

Immunoglobulins containing high levels of specific antibodies against hepatitis A have been used in some countries for passive immunisation against hepatitis A infection; in the UK, normal immunoglobulin is usually given.

Preparations

Ph. Eur.: Human Hepatitis A Immunoglobulin.

Proprietary Preparations (details are given in Part 3)
Port.: Globuman Hepatite A†.

Hepatitis A Vaccines

Vacunas de la hepatitis A.

ATC — J07BC02.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.

Ph. Eur. 6.2 (Hepatitis A Vaccine (Inactivated, Adsorbed); Vaccinum Hepatitidis A Inactivatum Adsorbatum; Inactivated Hepatitis A Vaccine BP 2008). A liquid preparation of a suitable strain of hepatitis A virus grown in cell cultures, inactivated by a validated method, and adsorbed on a mineral carrier. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light. The BP 2008 states that Hep A may be used on the label.

Ph. Eur. 6.2 (Hepatitis A Vaccine (Inactivated, Virosome); Vaccinum Hepatitidis A Inactivatum Virosomale). A liquid preparation of a suitable strain of hepatitis A virus grown in cell cultures and inactivated by a validated method. Virosomes composed of influenza proteins and phospholipids are used as adjuvants. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
The BP 2008 states that HepA may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

◊ General references.

1. Niu MT, *et al.* Two-year review of hepatitis A vaccine safety: data from the Vaccine Adverse Event Reporting System (VAERS). *Clin Infect Dis* 1998; **26:** 1475–6.

Effects on the blood. WHO has received reports of 5 cases of thrombocytopenia, 3 with purpura, associated with hepatitis A vaccine.[1]

1. Meyboom RHB, *et al.* Thrombocytopenia reported in association with hepatitis B and A vaccines. *Lancet* 1995; **345:** 1638.

Effects on the nervous system. Neurological symptoms resembling encephalitis have followed a third dose of hepatitis A vaccine.[1] Other serious neurological reactions reported in patients given inactivated hepatitis A vaccine include transverse myelitis, Guillain-Barré syndrome, and neuralgic amyotrophy.[2] Such reactions appear to be very rare, and, since other vaccines have often been given simultaneously, may not be directly attributable to hepatitis A vaccine.

1. Hughes PJ, *et al.* Probable post-hepatitis A vaccination encephalopathy. *Lancet* 1993; **342:** 302.
2. Committee on Safety of Medicines/Medicines Control Agency. Hepatitis A vaccination (Havrix). *Current Problems* 1994; **20:** 16.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Hepatitis A vaccines are used for active immunisation against hepatitis A infection.

In the UK, the use of an inactivated vaccine is recommended as an alternative to normal immunoglobulin for frequent travellers to areas of high or moderate hepatitis A endemicity or for those staying for more than 3 months in such areas; in some countries a hepatitis A immunoglobulin (p.2214) is available for those making shorter or less frequent journeys. Immunisation is also recommended in haemophiliacs, patients with chronic liver disease, and in those at risk of exposure to hepatitis A by virtue of their occupation, and should be considered in persons whose lifestyle is likely to place them at risk. The vaccine is given intramuscularly, except in haemophiliacs in whom it should be given by deep subcutaneous injection. In the UK, various vaccines are available and the dose (0.5 or 1 mL) depends on the product used and age of the patient. They may be prepared from several inactivated hepatitis A virus strains including CR326F, GBM, HM175, and RG-SB. The primary immunisation schedule for all vaccines consists of a single dose appropriate to the age of the patient and should be followed 6 to 12 months later by a booster dose. Immunity is provided for at least 10 years after these doses.

In the US, immunisation at 12 months of age (with a booster at least 6 months later) is recommended as part of the routine primary immunisation schedule. Post-exposure prophylaxis is recommended in persons who have not previously received a hepatitis A vaccine. Vaccination is also recommended for travellers to countries with intermediate to high hepatitis A endemicity.

◊ References.

1. American Academy of Pediatrics Committee on Infectious Diseases. Hepatitis A vaccine recommendations. *Pediatrics* 2007; **120:** 189–99. http://pediatrics.aappublications.org/cgi/reprint/120/1/189.pdf (accessed 15/07/08)

Vaccine development. Commercially available hepatitis A vaccines are usually produced from inactivated hepatitis A virus strains propagated in cell culture, commonly of human diploid fibroblast cells. 'Virosome' hepatitis A vaccines consisting of inactivated hepatitis A virus epitopes formulated into liposomes are also becoming available. Live attenuated hepatitis A vaccines have also been developed, although an oral live vaccine does not appear to have yet been produced.

Preparations

Ph. Eur.: Hepatitis A Vaccine (Inactivated, Adsorbed); Hepatitis A Vaccine (Inactivated, Virosome).

Proprietary Preparations (details are given in Part 3)
Arg.: Avaxim; Epaxal; Havrix; VAQTA; Virohep-A; ***Austral.:*** Avaxim; Havrix; VAQTA; ***Austria:*** Havrix; ***Belg.:*** Epaxal; Havrix; VAQTA†; ***Braz.:*** Avaxim†; Havrix†; Vacina Contra Hepatite A; VAQTA†; ***Canad.:*** Avaxim; Epaxal†; Havrix; VAQTA; ***Chile:*** Avaxim; Epaxal; Havrix; ***Cz.:*** Avaxim; Epaxal†; Havrix; VAQTA; ***Denm.:*** Epaxal; Havrix; ***Fin.:*** Epaxal; Havrix; VAQTA†; ***Fr.:*** Avaxim; Havrix; VAQTA†; ***Ger.:*** Epaxal†; Havpur; Havrix; VAQTA; ***Gr.:*** Avaxim; Epaxal; Havrix; VAQTA; ***Hong Kong:*** Avaxim; Epaxal; Havrix; VAQTA; ***Hung.:*** Avaxim; Havrix; VAQTA; ***India:*** Havrix; ***Indon.:*** Avaxim; Havrix; VAQTA; ***Irl.:*** Avaxim; Havrix; VAQTA†; ***Israel:*** Avaxim; Epaxal; Havrix; VAQTA; ***Ital.:*** Avaxim; Epaxal; Havrix; Nothav†; VAQTA; ***Malaysia:*** Avaxim; Epaxal; Havrix; VAQTA†; ***Mex.:*** Avaxim; Havrix; VAQTA; ***Neth.:*** Avaxim; Epaxal; Havrix; VAQTA; ***Norw.:*** Epaxal; Havrix; VAQTA†; ***NZ:*** Avaxim; Epaxal; Havrix; VAQTA; ***Philipp.:*** Avaxim; Epaxal; Havrix; ***Pol.:*** Avaxim; Havrix; VAQTA; ***Port.:*** Avaxim; Epaxal; Havrix; VAQTA; ***Rus.:*** Havrix (Хаврикс); VAQTA (ВАКТА); ***S.Afr.:*** Avaxim; Havrix; ***Singapore:*** Avaxim; Epaxal; Havrix; VAQTA; ***Spain:*** Avaxim; Epaxal; Havrix; VAQTA; ***Swed.:*** Avaxim; Epaxal; Havrix; VAQTA†; ***Switz.:*** Epaxal; Havrix; VAQTA†; ***Thai.:*** Avaxim; Havrix; VAQTA; ***Turk.:*** Avaxim; Epaxal; Havrix; VAQTA; ***UK:*** Avaxim; Epaxal; Havrix; VAQTA; ***USA:*** Havrix; VAQTA; ***Venez.:*** Epaxal†; Havrix.

Hepatitis B Immunoglobulins

Inmunoglobulinas contra la hepatitis B.

ATC — J06BB04.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii) and *US*, have monographs.

Ph. Eur. 6.2 (Human Hepatitis B Immunoglobulin; Immunoglobulinum Humanum Hepatitidis B). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from selected and/or immunised donors having specific antibodies against hepatitis B surface antigen. Normal immunoglobulin may be added. It contains not less than 100 international units/mL. The liquid preparation should be stored, protected from light, in a sealed, colourless, glass container. The freeze-dried preparation should be stored, protected from light, in a colourless, glass container, under vacuum or under an inert gas.

Ph. Eur. 6.2 (Human Hepatitis B Immunoglobulin for Intravenous Administration; Immunoglobulinum Humanum Hepatitidis B ad Usum Intravenosum). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from selected and/or immunised donors having antibodies against hepatitis B surface antigen. Human normal immunoglobulin for intravenous administration may be added. It contains not less than 50 international units/mL. Storage requirements are similar to those for Human Hepatitis B Immunoglobulin, except that the freeze-dried preparation is stored at a temperature not exceeding 25°.

USP 31 (Hepatitis B Immune Globulin). A is a sterile solution consisting of globulins derived from the plasma of human donors who have high titres of antibodies against hepatitis B surface antigen. It contains 10 to 18% of protein, of which not less than 80% is monomeric immunoglobulin G. It contains glycine as a stabilising agent, and a suitable preservative. It should be stored at 2° to 8°.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Preparation strength. For a warning concerning possible lack of equivalence between different preparations of hepatitis B immunoglobulins, see under Uses and Administration, below.