4 months to 5 years). It is not suitable for primary immunisation.

Preparations

Ph. Eur.: Diphtheria, Tetanus, Pertussis (Acellular, Component) and Poliomyelitis (Inactivated) Vaccine (Adsorbed); Diphtheria, Tetanus, Pertussis (Acellular, Component) and Poliomyelitis (Inactivated) Vaccine (Adsorbed, Reduced Antigen(s) Content); Diphtheria, Tetanus, Pertussis and Poliomyelitis (Inactivated) Vaccine (Adsorbed).

Proprietary Preparations (details are given in Part 3)
Austral.: Boostrix IPV; Infanrix IPV; Quadracel; ***Austria:*** Repevax; Tetravac; ***Belg.:*** Infanrix IPV; Tetracoq†; Tetravac; ***Braz.:*** Tetracoq†; Vacina Acel Ads Contra Dif, Tet, Coq e Polio Inat Comb C/Vac Conj Contra Hib; ***Canad.:*** Quadracel; ***Cz.:*** Infanrix Polio; ***Denm.:*** Di-Te-Ki-Pol; ***Fin.:*** Boostrix Polio; Di-Te-Ki-Pol†; Infanrix Polio; Tetravac; ***Fr.:*** Boostrixtetra; Infanrixtetra; Repevax; Tetravac; ***Ger.:*** Boostrix Polio; Quatro-Virelon†; Repevax; Tetravac†; ***Gr.:*** Boostrix Polio; Infanrix Tetra; Repevax; Tetracoq; Tetravac; ***Hung.:*** Tetraxim; ***Irl.:*** Tetravac; ***Israel:*** Tetracoq; ***Ital.:*** Tetravac; ***Malaysia:*** Infanrix IPV; Tetracoq†; Tetraxim; ***Mex.:*** Infanrix IPV; ***Neth.:*** Infanrix IPV; Triaxis; ***Norw.:*** Boostrix Polio; ***NZ:*** Boostrix IPV; Infanrix IPV; Quadracel; ***Philipp.:*** Tetracoq; Tetraxim; ***Pol.:*** DTaP-IPV; Tetracoq†; ***Port.:*** Boostrix Polio; Infanrix Tetra; Repevax; Tetravac; ***Swed.:*** Boostrix Polio; Di-Te-Ki-Pol†; Tetravac; ***Switz.:*** Boostrix Polio; Infanrix DTPa-IPV; Tetravac; ***Thai.:*** Tetracoq†; Tetraxin; ***Turk.:*** Tetracoq; ***UK:*** Infanrix IPV; Repevax; ***Venez.:*** Vacuna Adsorbida Tetravalente.

Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Haemophilus Influenzae Vaccines

Vacunas de la difteria, el tétanos, la tos ferina, la poliomielitis y Haemophilus influenzae.

ATC — J07CA06.

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

Ph. Eur. 6.2 (Diphtheria, Tetanus, Pertussis (Acellular, Component), Poliomyelitis (Inactivated) and Haemophilus type b Conjugate Vaccine (Adsorbed); Vaccinum Diphtheriae, Tetani, Pertussis Sine Cellulis ex Elementis Praeparatum Poliomyelitidis Inactivatum et Haemophili Stirpe b Conjugatum Adsorbatum). A combined vaccine composed of diphtheria formol toxoid, tetanus formol toxoid, individually purified antigenic components of *Bordetella pertussis*, suitable strains of human polioviruses type 1, 2, and 3 grown in suitable cell cultures and inactivated by a validated method, polyribosylribitol phosphate derived from a suitable strain of *Haemophilus influenzae* type b and covalently bound to a carrier protein, and a mineral carrier such as aluminium hydroxide or hydrated aluminium phosphate. The product is presented with the Haemophilus type b component in a separate container, the contents of which are mixed with the other components immediately before use. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

Ph. Eur. 6.2 (Diphtheria, Tetanus, Pertussis, Poliomyelitis (Inactivated) and Haemophilus type b Conjugate Vaccine (Adsorbed); Vaccinum Diphtheriae, Tetani, Pertussis, Poliomyelitidis Inactivatum et Haemophili Stirpe b Conjugatum Adsorbatum). A combined vaccine composed of diphtheria formol toxoid, tetanus formol toxoid, an inactivated suspension of *Bordetella pertussis*, suitable strains of human polioviruses type 1, 2, and 3 grown in suitable cell cultures and inactivated by a validated method, polyribosylribitol phosphate derived from a suitable strain of *Haemophilus influenzae* type b and covalently bound to a carrier protein, and a mineral carrier such as aluminium hydroxide or hydrated aluminium phosphate. The product is presented with the Haemophilus type b component in a separate container, the contents of which are mixed with the other components immediately before use. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

See also under Diphtheria Vaccines, p.2209, Diphtheria, Tetanus, and Pertussis Vaccines, p.2210, Haemophilus Influenzae Vaccines, p.2213, Pertussis Vaccines, p.2230, and Tetanus Vaccines, p.2240.

Premature neonates. In an observational study[1] of 78 very-low-birth-weight premature neonates given a combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and Haemophilus influenzae vaccine before hospital discharge, increased incidences of apnoea, bradycardia, desaturation, or oxygen requirement occurred in 47% overall within 24 to 48 hours of vaccination. All neonates with increased events returned to baseline within 48 to 72 hours and there was no detrimental impact on clinical course. The authors considered that, although monitoring and appropriate intervention were required, delaying vaccination was not warranted, a view in line with UK and USA official recommendations (see p.2202).

1. Pfister RE, *et al.* Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* 2004; **145:** 58–66.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

A combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and Haemophilus influenzae vaccine is used for active immunisation of children. For discussion of immunisation schedules, see under Vaccines, p.2202.

In the UK it is used as part of the recommended schedule for primary immunisation. It is given by intramuscular injection in usual doses of 0.5 mL; three doses are given at intervals of one month, starting preferably at 2 months of age. Although it is not licensed for use after a child's fourth birthday, the national schedule considers it may be used up to the age of 10 years.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Pentaxim; Poliacel†; ***Austral.:*** Pediacel; Poliacel; ***Austria:*** Infanrix IPV + Hib; ***Belg.:*** Infanrix IPV + Hib†; ***Braz.:*** Infanrix IPV + Hib†; Pentact-HIB†; Poliacel†; Vacina Comb. Contra Dif.-Tet.-Pert. Acel, Polio Inat e HIB; ***Canad.:*** Pentacel; ***Chile:*** Pentact-HIB; ***Cz.:*** Infanrix IPV + Hib; ***Denm.:*** Di-Te-Ki-Pol/Act-Hib; ***Fin.:*** Infanrix Polio + Hib; Pentavac; ***Fr.:*** Infanrixquinta; Pentacoq†; Pentavac; ***Ger.:*** Infanrix IPV + Hib; Pentavac; ***Gr.:*** Infanrix IPV + Hib; Pentavac; ***Hong Kong:*** Infanrix IPV + Hib; Pentact-HIB; ***Hung.:*** Infanrix IPV + Hib; Pentaxim; ***Irl.:*** Infanrix IPV + Hib; Pentavac; ***Israel:*** Infanrix Polio IPV - Hib; Pentact-HIB; Poliacel-Act-Hib; ***Ital.:*** Cinquerix†; Pentavac; Quinivaxin†; ***Malaysia:*** Infanrix IPV + Hib; Pediacel; Pentaxim; ***Mex.:*** Infanrix IPV + Hib; Pediacel; ***Neth.:*** DKTP-Hib; Infanrix IPV + Hib; Pediacel; ***Norw.:*** Infanrix Polio + Hib; ***NZ:*** Infanrix IPV + Hib; ***Philipp.:*** Pentact-HIB; Pentaxim; ***Pol.:*** Infanrix IPV + Hib; Pentaxim; ***Port.:*** Infanrix IPV + Hib; Pediacel; ***S.Afr.:*** Pentact-HIB†; ***Singapore:*** Infanrix IPV + Hib; ***Spain:*** Pentavac; ***Swed.:*** Infanrix Polio + Hib; Pentavac; ***Switz.:*** Infanrix DTPa-IPV+Hib; Pentavac; ***Thai.:*** Infanrix IPV + Hib; Pediacel; Pentact-HIB†; Pentaxim; ***Turk.:*** Infanrix IPV-HIB; Pentact-HIB; Poliacel; ***UK:*** Infanrix IPV + Hib; Pediacel; ***Venez.:*** Infanrix IPV + Hib; Vacuna Adsorbida Pentavalente.

Diphtheria, Tetanus, Pertussis, Poliomyelitis, and Hepatitis B Vaccines

ATC — J07CA12.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

See also under Diphtheria Vaccines, p.2209, Diphtheria, Tetanus, and Pertussis Vaccines, p.2210, Hepatitis B Vaccines, p.2215, Pertussis Vaccines, p.2230, and Tetanus Vaccines, p.2240.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

A combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and hepatitis B vaccine is available in some countries for active immunisation of children.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Infanrix Penta; ***Cz.:*** Infanrix Penta; ***Gr.:*** Infanrix Penta; ***Ital.:*** Infanrix Penta; ***Neth.:*** Infanrix Penta; ***NZ:*** Infanrix Penta; ***Port.:*** Infanrix Penta; ***USA:*** Pediarix.

Diphtheria, Tetanus, and Poliomyelitis Vaccines

Vacunas de la difteria, el tétanos y la poliomielitis.

ATC — J07CA01.

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

Ph. Eur. 6.2 (Diphtheria, Tetanus and Poliomyelitis (Inactivated) Vaccine (Adsorbed, Reduced Antigens(s) Content); Vaccinum Diphtheriae, Tetani et Poliomyelitidis Inactivatum, Antigeni-o(-is) Minutum, Adsorbatum). A combined vaccine containing diphtheria formol toxoid, tetanus formol toxoid, suitable strains of human polioviruses types 1, 2, and 3 grown in suitable cell cultures and inactivated by a validated method, and a mineral adsorbent such as aluminium hydroxide or hydrated aluminium phosphate. The amount of diphtheria toxoid per single human dose is reduced compared to vaccines generally used for primary vaccination; the amount of tetanus toxoid may also be reduced. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

See also under Diphtheria Vaccines, p.2209, Diphtheria and Tetanus Vaccines, p.2210, and Tetanus Vaccines, p.2240.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

A combined diphtheria, tetanus, and poliomyelitis (inactivated) vaccine is used for active immunisation. For discussion of immunisation schedules see under Vaccines, p.2202.

In the UK it is used as part of the recommended schedule and is given by intramuscular injection in a single dose (usually 0.5 mL) as a booster at the ages of 13 to 18 years. It is not licensed for primary immunisation.

Preparations

Ph. Eur.: Diphtheria, Tetanus, and Poliomyelitis (Inactivated) Vaccine (Adsorbed, Reduced Antigen(s) Content).

Proprietary Preparations (details are given in Part 3)
Austria: Revaxis; ***Belg.:*** Revaxis; ***Canad.:*** Td-Polio; ***Fr.:*** DT Polio; Revaxis; Vaccin DTP†; ***Ger.:*** Revaxis; Td-Virelon; ***Gr.:*** Revaxis; ***Hung.:*** Dultavax; ***Irl.:*** Revaxis; ***Ital.:*** Revaxis; ***Neth.:*** Revaxis; ***Port.:*** Revaxis; ***Switz.:*** Revaxis; Td-Virelon; ***UK:*** Revaxis.

Endotoxin Antibodies

Anticuerpos antiendotoxinas.

Profile

Antibodies against the endotoxin of Gram-negative bacteria have been tried as adjunctive therapy for the treatment and prevention of Gram-negative bacteraemia and shock.

Early preparations consisted of antisera prepared from the sera of donors immunised with *Escherichia coli* J5; these were superseded by human and murine IgM monoclonal antibodies. Nebacumab (HA-1A) is a human monoclonal IgM antibody that binds specifically to the lipid A domain of endotoxin. Lipid A in the circulation releases tumour necrosis factor and other cytokines from macrophages and endothelial cells which may ultimately culminate in physiological effects such as multiple organ failure. Despite early promising results of clinical studies the safety of nebacumab in patients without Gram-negative septicaemia was questioned and the product was withdrawn.

A murine monoclonal IgM antibody (edobacomab; E5) has also undergone clinical trials although results have been disappointing.

Epstein-Barr Virus Vaccines

Vacunas del virus de Epstein-Barr.

Profile

Several Epstein-Barr virus vaccines are under investigation for active immunisation against infectious mononucleosis and post-transplant lymphoproliferative disorders.

◊ Epstein-Barr virus is a herpesvirus that is ubiquitous in the adult population. It only causes clinical illness where primary infection occurs in adolescence or adulthood, when it prompts the symptoms of infectious mononucleosis in about 50% of cases. More than 90% of the world's population, however, carry the virus as a lifelong latent infection of B-lymphocytes and, as a result, Epstein-Barr virus can also be associated with malignancies including lymphoproliferative diseases, Burkitt's lymphoma, gastric carcinoma, oral hairy leucoplakia, nasopharyngeal carcinoma, and Hodgkin's disease.

Vaccines against Epstein-Barr virus infection are under investigation[1,2] and the main focus has been towards the development of a vaccine to prevent primary infection or to minimise its consequences, namely infectious mononucleosis and post-transplant lymphoproliferative disease, rather than towards the malignancies associated with the virus which occur in relatively fewer patients. Two main approaches have been adopted, the first of which seeks to exploit the major envelope glycoprotein of the virus, gp340, because of its ability to induce neutralising antibodies. This vaccine may prevent infectious mononucleosis by moderating the initial viral replication and spread during primary infection, thereby curtailing the cytotoxic T-lymphocyte response to lytic antigens that would otherwise invoke the immunological processes responsible for clinical symptoms. The second approach is based on the induction of cytotoxic T-cells specific to Epstein-Barr virus, thereby aiming to reduce the clinical symptoms of infectious mononucleosis rather than to prevent primary infection.

Potential future vaccines for malignancies associated with Epstein-Barr virus are likely to be therapeutic rather than preventative and to exploit the presence of the virus in tumour cells; alternatively they may be focussed on tumour antigens not encoded by Epstein-Barr virus.[1,2]

1. Moss DJ, *et al.* Candidate vaccines for Epstein-Barr virus. *BMJ* 1998; **317:** 423–4.
2. Macsween KF, Crawford DH. Epstein-Barr virus—recent advances. *Lancet Infect Dis* 2003; **3:** 131–40.

Escherichia Coli Vaccines

Vacunas de Escherichia coli.

Profile

Vaccines against enterotoxigenic strains of *Escherichia coli* are under investigation. Vaccine candidates include toxoids, inactivated whole bacteria, purified surface antigens, and live oral vaccines.

◊ Infectious diarrhoea remains a major source of morbidity and mortality in the world and a significant proportion is caused by pathogenic strains of *Escherichia coli* While it is considered feasible to develop effective vaccines against *E. coli*, at present there are no such vaccines available. Current approaches against enteropathogenic *E. coli* (EPEC) and enterohaemorrhagic *E. coli* (EHEC) have focussed on three main areas: the EPEC and EHEC proteins involved in colonisation of the intestine, the EHEC O157-specific side-chain of lipopolysaccharides, and the

immunogenicity of Shiga toxin produced by the organism. While vaccination against EPEC has to be directed towards susceptible human populations, there are two possible approaches with regard to EHEC, namely vaccination of either humans or the animal reservoir, cattle. Studies of vaccine candidates are ongoing *in vitro*, in *animal* models, and in healthy subjects. For both pathogens, however, the development of vaccines would not in itself serve to eradicate the spread of infections and would need to be accompanied by public health campaigns to increase food hygiene and monitoring of water supplies and facilities.[1]

Enterotoxigenic *E. coli* (ETEC) is a major cause of travellers' diarrhoea. A phase II placebo-controlled study[2] found that a vaccine containing heat-labile enterotoxin from ETEC given as a skin patch (2 patches applied 2 to 3 weeks apart), reduced the risk of moderate to severe travellers' diarrhoea by 75% and severe diarrhoea by 84%. In vaccinated travellers who got diarrhoea, the illness was significantly shorter and milder.

Further references.[3-7]

1. Horne C, *et al.* Current progress in enteropathogenic and enterohemorrhagic Escherichia coli vaccines. *Expert Rev Vaccines* 2002; **1:** 483–93.
2. Frech SA, *et al.* Use of a patch containing heat-labile toxin from Escherichia coli against travellers' diarrhoea: a phase II, randomised, double-blind, placebo-controlled field trial. *Lancet* 2008; **371:** 2019–25.
3. Boedeker EC. Vaccines for enterotoxigenic Escherichia coli: current status. *Curr Opin Gastroenterol* 2005; **21:** 15–9.
4. Steffen R, *et al.* Vaccination against enterotoxigenic Escherichia coli, a cause of travelers' diarrhea. *J Travel Med* 2005; **12:** 102–7.
5. Walker RI, *et al.* Ad Hoc ETEC Technical Expert Committee. Analysis of strategies to successfully vaccinate infants in developing countries against enterotoxigenic E. coli (ETEC) disease. *Vaccine* 2007; **25:** 2545–66.
6. Goldwater PN. Treatment and prevention of enterohemorrhagic Escherichia coli infection and hemolytic uremic syndrome. *Expert Rev Anti Infect Ther* 2007; **5:** 653–63.
7. Serna A, Boedeker EC. Pathogenesis and treatment of Shiga toxin-producing Escherichia coli infections. *Curr Opin Gastroenterol* 2008; **24:** 38–47.

Gas-gangrene Antitoxins

Antitoxinas de la gangrena gaseosa.

ATC — J06AA05.

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

Ph. Eur. 6.2 (Gas-gangrene Antitoxin (Novyi); Immunoserum Gangraenicum (Clostridium Novyi)). A sterile preparation containing the specific antitoxic globulins that have the power of neutralising the alpha toxin formed by *Clostridium novyi*. It has a potency of not less than 3750 international units/mL. It should be stored at 2° to 8°, and not be allowed to freeze.

The BP 2008 states that Nov/Ser may be used on the label.

The BP 2008 gives Gas-gangrene Antitoxin (Oedematiens) as an approved synonym.

Ph. Eur. 6.2 (Gas-gangrene Antitoxin (Perfringens); Immunoserum Gangraenicum (Clostridium Perfringens)). A sterile preparation containing the specific antitoxic globulins that have the power of neutralising the alpha toxin formed by *Clostridium perfringens*. It has a potency of not less than 1500 international units/mL. It should be stored at 2° to 8°, and not be allowed to freeze.

The BP 2008 states that Perf/Ser may be used on the label.

Ph. Eur. 6.2 (Gas-gangrene Antitoxin (Septicum); Immunoserum Gangraenicum (Clostridium Septicum)). A sterile preparation containing the specific antitoxic globulins that have the power of neutralising the alpha toxin formed by *Clostridium septicum*. It has a potency of not less than 1500 international units/mL. It should be stored at 2° to 8°, and not be allowed to freeze.

The BP 2008 states that Sep/Ser may be used on the label.

Ph. Eur. 6.2 (Gas-gangrene Antitoxin, Mixed; Immunoserum Gangraenicum Mixtum). It is prepared by mixing Gas-gangrene Antitoxin (Novyi), Gas-gangrene Antitoxin (Perfringens), and Gas-gangrene Antitoxin (Septicum) in appropriate quantities. It has a potency of not less than 1000 international units/mL of Gas-gangrene Antitoxin (Novyi), not less than 1000 international units/mL of Gas-gangrene Antitoxin (Perfringens), and not less than 500 international units/mL of Gas-gangrene Antitoxin (Septicum). It should be stored at 2° to 8°, and not be allowed to freeze.

The BP 2008 states that Gas/Ser may be used on the label.

Profile

Gas-gangrene antitoxins have been used for the treatment of gas gangrene and for prophylaxis in patients at risk after injury. They are now seldom used and have been superseded by antibacterials. Monovalent gas-gangrene antitoxins have been little used in practice owing to the difficulty of rapidly identifying the infecting organism.

Preparations

Ph. Eur.: Gas-gangrene Antitoxin (Novyi); Gas-gangrene Antitoxin (Perfringens); Gas-gangrene Antitoxin (Septicum); Mixed Gas-gangrene Antitoxin.

Proprietary Preparations (details are given in Part 3)

Cz.: Gasea†.

Gonococcal Vaccines

Gonorrhoea Vaccines; Vacunas de la gonorrea.

Profile

Several experimental gonococcal vaccines, produced usually from the surface antigens of *Neisseria gonorrhoeae*, have been investigated.

Haemophilus Influenzae Vaccines

Vacunas de Haemophilus influenzae.

ATC — J07AG01 (B, purified antig. conjugate).

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

Ph. Eur. 6.2 (Haemophilus type b Conjugate Vaccine; Vaccinum Haemophili Stirpe B Conjugatum). A liquid or freeze-dried preparation of a polysaccharide, polyribosylribitol phosphate (PRP), derived from a suitable strain of *Haemophilus influenzae* type b, covalently bound to a carrier protein. The carrier protein, when conjugated to PRP, is capable of inducing a T-cell-dependent B-cell immune response to the polysaccharide. Carrier proteins currently approved are diphtheria toxoid, tetanus toxoid, CRM 197 diphtheria protein, and meningococcal group B outer membrane protein (OMP). It should be stored at 2° to 8° and protected from light.

The BP 2008 states that Hib may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Erythema multiforme and transient cyanosis of the lower limbs have been reported rarely in children receiving haemophilus influenzae-containing vaccines.

Effects on the nervous system. Guillain-Barré syndrome has been reported[1] after vaccination with haemophilus influenzae conjugate vaccines in a small number of infants. In one report, onset of symptoms occurred within 1 week of vaccination of 3 infants with an haemophilus influenzae conjugate vaccine (diphtheria toxoid conjugate). However, a causal relationship has not yet been established.

1. D'Cruz OF, *et al.* Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome) after immunization with Haemophilus influenzae type b conjugate vaccine. *J Pediatr* 1989; **115:** 743–6.

Interactions

As for vaccines in general, p.2202.

Antineoplastics. Haemophilus influenzae infection occurred in a child who had received antineoplastic therapy despite having completed a primary course of immunisation before the neoplasia was diagnosed.[1] A subsequent booster dose produced an adequate antibody response. Antineoplastic therapy may have impaired the T-cell response to infection.

1. Jenkins DR, *et al.* Childhood neoplasia and Haemophilus influenzae type b vaccine failure. *Lancet* 1996; **348:** 131.

Diphtheria, tetanus, and pertussis vaccines. Some haemophilus influenzae conjugated vaccines may be mixed with diphtheria, tetanus, and pertussis vaccines before administration without adversely affecting the immunogenicity of the components[1,2] although there has also been a report of reduced immunogenicity.[3] Manufacturers may provide further information on compatibility.

1. Miller MA, *et al.* Safety and immunogenicity of PRP-T combined with DTP: excretion of capsular polysaccharide and antibody response in the immediate post-vaccination period. *Pediatrics* 1995; **95:** 522–7.
2. Mulholland EK, *et al.* The use of Haemophilus influenzae type b-tetanus toxoid conjugate vaccine mixed with diphtheria-tetanus-pertussis vaccine in Gambian infants. *Vaccine* 1996; **14:** 905–9.
3. Eskola J, *et al.* Randomised trial of the effect of co-administration with acellular pertussis DTP vaccine on immunogenicity of Haemophilus influenzae type b conjugated vaccine. *Lancet* 1996; **348:** 1688–92.

Uses and Administration

Haemophilus influenzae (Hib) vaccines are used for active immunisation against *Haemophilus influenzae* type b infections. Vaccines are prepared from the capsular polysaccharide of *H. influenzae* type b and immunogenicity, especially in young children, is improved by linking the polysaccharide to a protein carrier to form a conjugate vaccine.

Different proprietary vaccines may be conjugated to differing proteins but are generally regarded as interchangeable.

Haemophilus Influenzae Conjugate Vaccine (Diphtheria Toxoid Conjugate) (PRP-D) consists of the purified capsular polysaccharide of *Haemophilus influenzae* type b covalently linked to diphtheria toxoid.

Haemophilus Influenzae Conjugate Vaccine (Diphtheria CRM_{197} Protein Conjugate) (HbOC) consists of oligosaccharides derived from the purified capsular polysaccharide of *Haemophilus influenzae* type b covalently linked to a non-toxic variant of diphtheria toxin isolated from *Corynebacterium diphtheriae*.

Haemophilus Influenzae Conjugate Vaccine (Meningococcal Protein Conjugate) (PRP-OMP or PRP-OMPC) consists of the purified capsular polysaccharide of *Haemophilus influenzae* type b covalently linked to an outer membrane protein complex of *Neisseria meningitidis* group B.

Haemophilus Influenzae Conjugate Vaccine (Tetanus Toxoid Conjugate) (PRP-T) consists of the purified capsular polysaccharide of *Haemophilus influenzae* type b covalently linked to tetanus toxoid.

For primary immunisation either combined vaccines or single-component Haemophilus influenzae vaccines may be used.

In the UK, a combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and Haemophilus influenzae vaccine (p.2212) is used. Children over 1 year of age and under 10 years of age who have not been immunised against *Haemophilus influenza* or have not completed a primary vaccination course of diphtheria, tetanus, pertussis, or polio, should be given 3 doses of a combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and *Haemophilus influenzae* vaccine. Those who have completed a primary vaccination course of diphtheria, tetanus, pertussis, and polio, should receive a single dose of a combined *Haemophilus influenzae* and meningococcal C conjugate vaccine. Routine use in children older than 10 years or adults is not recommended in the UK, but asplenic children (over 10 years of age) and adults who have not been previously immunised should receive two doses of combined *Haemophilus influenzae* and meningococcal C conjugate vaccine, two months apart.

In the USA, primary immunisation is also carried out in conjunction with diphtheria, tetanus, and pertussis vaccination. If a meningococcal protein conjugate vaccine is used, only 2 doses are given for the primary course. A reinforcing dose using any of the available vaccines is given at 12 to 15 months of age.

Where compatibility has been shown, Hib vaccines may be mixed immediately before use with diphtheria, tetanus, and pertussis vaccines (but see Interactions, above).

Preparations

Ph. Eur.: Haemophilus Type b Conjugate Vaccine.

Proprietary Preparations (details are given in Part 3)

Arg.: PedvaxHIB†; ***Austral.:*** Hiberix; HibTITER†; PedvaxHIB; ***Austria:*** Act-HIB; HibTITER; ***Belg.:*** Act-HIB; Hiberix†; HibTITER†; ***Braz.:*** Act-HIB†; Hiberix†; PedvaxHIB; Vacina Conj Com Proteina Tetanica Contra Haemophilus influenzae Tipo B; Vacina Conj Contra Haemophilus Influenzae Tipo B; ***Canad.:*** Act-HIB; PedvaxHIB; ***Chile:*** Act-HIB; ***Cz.:*** Act-HIB; Hiberix; HibTITER†; ***Denm.:*** Act-HIB; HibTITER†; ***Fin.:*** Hiberix†; HibTITER†; ***Fr.:*** Act-HIB; ***Ger.:*** Act-HIB†; HibTITER†; PedvaxHIB†; ***Gr.:*** Act-HIB; Hiberix; HibTITER†; ***Hong Kong:*** Act-HIB; Hiberix; PedvaxHIB; ***Hung.:*** Act-HIB; ***India:*** Hiberix; Vaxim HIB; ***Indon.:*** Act-HIB; Hiberix; PedvaxHIB; ***Irl.:*** Act-HIB; Hiberix; HibTITER†; ***Israel:*** Act-HIB; HibTITER†; PedvaxHIB†; ***Ital.:*** Act-HIB; Hiberix; HibTITER†; Vaxem Hib; ***Malaysia:*** Act-HIB†; Hiberix; PedvaxHIB†; ***Mex.:*** HibTITER†; PedvaxHIB; Vaxem Hib†; ***Neth.:*** Act-HIB; Hiberix; ***Norw.:*** Act-HIB; ***NZ:*** Hiberix; HibTITER†; ***Philipp.:*** Act-HIB; Hiberix; Vaxem Hib; ***Pol.:*** Act-HIB; Hiberix; HibTITER; PedvaxHIB; ***Port.:*** Hiberix; HibTITER†; ***Rus.:*** Hiberix (Хиберикс); ***S.Afr.:*** Act-HIB; Hiberix; ***Singapore:*** Act-HIB; Hiberix; PedvaxHIB†; ***Spain:*** Act-HIB; Hiberix; HibTITER; ***Swed.:*** Act-HIB; HibTITER†; ***Switz.:*** Hiberix; ***Thai.:*** Act-HIB; Hiberix; PedvaxHIB; Vaxem Hib; ***Turk.:*** Act-HIB; Hiberix; PedvaxHIB; ***UK:*** Act-HIB†; Hiberix; ***USA:*** Act-HIB; HibTITER; OmniHIB; PedvaxHIB; ProHIBiT†; ***Venez.:*** Act-HIB†; Hiberix.

Haemophilus Influenzae and Hepatitis B Vaccines

Vacunas de Haemophilus influenzae y la hepatitis B.

ATC — J07CA08.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Haemophilus influenzae type b (Hib) conjugate and hepatitis B vaccines are available in some countries for active immunisation as part of the primary immunisation of infants born to HBsAg-negative mothers. In the USA, an Haemophilus influenzae type b conjugate (meningococcal protein conjugate) and hepatitis B (recombinant) vaccine is used. It is given in a schedule of 3 doses, 0.5 mL being given intramuscularly at 2 months, 4 months, and 12 to 15 months of age. Use in infants less than 6 weeks old is not recommended.