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