28a

Shingles (herpes zoster)

The disease

Shingles (herpes zoster) is caused by the reactivation of a latent varicella zoster virus (VZV) infection, generally decades after the primary infection.

Primary VZV infection typically occurs during childhood and causes chickenpox (varicella); further information on this can be found in Chapter 34. Following primary VZV infection, the virus enters the sensory nerves and travels along the nerve to the sensory dorsal root ganglia and establishes a permanent latent infection. Reactivation of the latent virus leads to the clinical manifestations of shingles, and is associated with immune senescence or suppression of the immune system i.e. immunosuppressive therapy, HIV infection, malignancy and/or increasing age. The annual incidence of shingles for those aged 70 to 79 years is estimated to be around 790 to 880 cases per 100,000 people in England and Wales (van Hoek *et al*., 2009), see Figure 1.The risk and severity of shingles increases with age.

The first signs of shingles begin most commonly with abnormal skin sensations and pain in the affected area of skin (dermatome). Headache, photophobia, malaise and less commonly fever may occur as part of the prodromal phase. Within days or weeks, a unilateral vesicular (fluid filled blisters) rash typically appears in a dermatomal distribution. In immunocompromised individuals, a rash involving multiple dermatomes may occur. The affected area may be intensely painful with associated paraesthesia (tingling, pricking, or numbness of the skin), and intense itching is common (Gilden *et al*., 1991). The rash typically lasts between two and four weeks.

Following the rash, persistent pain at the site, known as Post Herpetic Neuralgia (PHN), can develop and is seen more frequently in older people. Pain that persists for, or appears more than 90 days after the onset of rash (Oxman *et al*., 2005) is a commonly accepted definition for PHN. On average, PHN lasts from three to six months, but can persist for longer. The severity of pain can vary and may be constant, intermittent or triggered by stimulation of the affected area, such as by wind on the face. (Katz *et al*., 2004)

Other complications of shingles depend on the nerves affected and include paresis (motor weakness), facial palsy and 'herpes zoster ophthalmicus', with involvement of the eye and associated dermatome, which may result in keratitis, corneal ulceration, conjunctivitis, retinitis, optic neuritis and/or glaucoma. (Shaikh S *et al*., 2002; Pavan LD, 1995)

The reactivated virus can, in some cases, disseminate into the lungs, liver, gut, and brain, leading to pneumonia, hepatitis, encephalitis, and disseminated intravascular coagulopathy. Disseminated disease is more likely to occur in those who are severely immunocompromised, with a case fatality rate reported to be between 5 and 15%, and most deaths being attributable to pneumonia (Rogers *et al*., 1995; Gnann *et al*., 1991).

Individuals with active lesions, particularly if they are immunosuppressed, can transmit VZV to susceptible individuals to cause chickenpox and therefore at risk individuals who have had a significant exposure to shingles require post exposure management (see **Chapter 34**). There is no evidence that shingles can be acquired from another individual who has chickenpox.

History and epidemiology of the disease

Varicella infection is a prerequisite for the development of shingles. In temperate climates in the absence of a varicella vaccination programme, the lifetime risk for varicella infection is over 95% (Banz *et al*., 2003).

Although shingles can occur at any age, incidence increases with age (see Figure 1) with an estimated lifetime risk of one in four, (Miller *et al*., 1993). The increasing incidence with age is thought to be associated with age related immune senescence.

Age-specific incidence rates of shingles have been estimated using a number of different primary care derived data sources (van Hoek *et al*., 2009).

Data from GP-based studies in England and Wales suggest that over 50,000 cases of shingles occur in older people aged 70 years and over annually. The severity of shingles generally increases with age (Figure 1) and can lead to PHN that can require hospitalisation (Table 1). Studies have estimated ophthalmic zoster to occur in 10-20% of shingles cases (Opstelten *et al*., 2002) with around 4% of the cases resulting in long-term sequelae, including pain (Bowsher,1999).

It is estimated that, in people aged 70 years and over, around one in 1000 cases of shingles results in death (van Hoek *et al*., 2009), although due to the nature

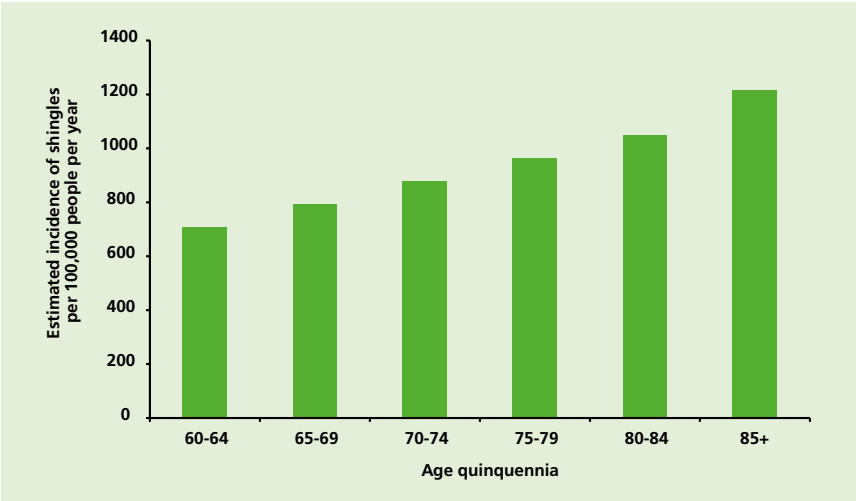

Figure 28a.1 Estimated annual age-specific incidence of shingles per 100,000 per year in the immunocompetent population in England and Wales (population 2007). Data taken from van Hoek et al., 2009.

Table 28a 1: Estimated percentage developing PHN by age group in the immunocompetent population in England and Wales (population 2007). Data taken from van Hoek et al., 2009.

	Age group					
	60-64 years	65-69 years	70-74 years	75-79 years	80-84 years	85 years
Proportion developing PHN after 90 days	9%	11%	15%	20%	27%	52%

of the population and risk of co-morbidities some deaths recorded as being shingles related may not be directly attributable to the disease.

The risk of shingles is also increased in individuals with certain conditions, including systemic lupus erythematosus, (Nagasawa *et al*.,1990) rheumatoid arthritis, (Smitten *et al*., 2007), diabetes (Heymann *et al* 2008) and Wegener's granulomatosis. (Wung *et al*., 2005).

The shingles vaccination

Zostavax® is the only market authorised shingles vaccine available in the UK. It contains live, attenuated virus derived from the Oka/Merck strain of varicella zoster virus, at a significantly higher dose than the Varivax® varicella vaccine.

In a clinical trial, one dose of Zostavax® was assessed in 38,546 adults aged 60 years and over of whom 17,775 were aged 70 years or over. The Zostavax® vaccine reduced the incidence of shingles in those aged 60 years and over and in those aged 70 years and over by 51.3% and 38% respectively, and the incidence of PHN by 66.5% and 66.8% respectively (Oxman *et al*., 2005; Oxman *et al*., 2008). The vaccine is well tolerated and is also immunogenic in individuals who have had a history of shingles prior to vaccination (Levin *et al*., 2008).

In clinical trials with Zostavax®, transmission of the vaccine virus has not been reported. However, experience with varicella vaccines which use a lower dose of the same virus strain suggests that transmission of vaccine virus occur rarely between those vaccinees that develop a varicella-zoster virus (VZV)-like rash and susceptible close contacts. Transmission of vaccine virus from varicella vaccine recipients without VZV-like rash has not been confirmed. Whilst there remains a theoretical risk, therefore, in those who develop a rash following zoster vaccination of transmitting the attenuated vaccine virus to a susceptible individual , this risk should be weighed against the reduced risk of developing natural shingles and the much higher risk of transmission from the circulating wild type VZV in the community.

The full duration of protection following a single dose of Zostavax® is not known. In the original clinical trials the average follow up was 3.09 years although it is likely that the vaccine confers protection for longer. The latest data (Schmader *et al.,* 2010) shows the vaccine to be effective at least 5 years post vaccination and follow up is continuing. The need for, or timing of, revaccination with Zostavax® has therefore not yet been determined.

Storage

The unreconstituted vaccine and its diluent should be stored in the original packaging at +2°C to +8°C and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Effectiveness may be reduced unless the vaccine is stored at the correct temperature. Freezing may cause increased reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents.

Presentation

Zostavax® is available as a lyophilised preparation (an off-white compact crystalline plug) for reconstitution with a diluent (a clear colourless fluid). When reconstituted, Zostavax® is a semi-hazy to translucent, off-white to pale yellow liquid.

Zostavax® is supplied as a vial and a prefilled syringe, with two separate needles in the secondary packaging. Zostavax® is only available in single packs.

After reconstitution of the lyophilised suspension, the vaccine should be used immediately, but may be used up to 30 minutes following reconstitution.

Dosage and schedule

Adults should receive a single **0.65ml** dose of Zostavax®

The need for and timing of reinforcing doses have not yet been determined.

Administration

Zostavax® may be administered by intramuscular or subcutaneous injection, preferably in the deltoid region of the upper arm. Intramuscular injection is the preferred route of administration, as injection-site adverse reactions were significantly less frequent in those who received the vaccine via this route of administration. For individuals with a bleeding disorder, Zostavax® should be given by deep subcutaneous injection to reduce the risk of bleeding. The vaccine must not be given intravascularly. Further information on injection technique can be found in Chapter 4.

Zostavax® can be given at the same time as inactivated influenza vaccination. If given at the same time as influenza vaccination, care should be taken to ensure that the appropriate route of injection is used for all the vaccinations.

Whether administered at the same time as other vaccines or separately, as the eligible population are likely to have a high prevalence of co-morbidity, it is important to check that the recipient has no contraindications to administering a live vaccine.

Zostavax® can be given at the same time as 23-valent pneumococcal polysaccharide vaccine for those who are eligible for both vaccines. Although a single manufacturer-conducted trial showed inferior VZV antibody responses in those receiving zoster vaccine and PPV-23 concomitantly compared with those receiving the vaccines four weeks apart, there is no established correlation between antibody titres to VZV and protection from herpes zoster.

Furthermore, a more recent observational study showed that herpes zoster vaccine was equally effective at preventing herpes zoster whether it was administered at the same time or four weeks apart from PPV-23 (Tseng *et al*.,2011).

The vaccines should be given at separate sites, preferably in different limbs. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2006). The site at which each vaccine was given should be noted in the individual's records.

Based on evidence that MMR vaccine can lead to an attenuation of the varicella vaccine response (Mullooly *et al*., 2001), it is recommended that, a four-week interval is observed between administration of MMR and Zostavax® vaccines to ensure adequate protection.

Travel vaccines containing live attenuated virus e.g. yellow fever, may be given to the age group recommended for shingles vaccination. There is limited evidence on the timing of administration of Zostavax and Yellow Fever vaccine, with a single case report demonstrating good response to Yellow Fever vaccine 21 days after receiving Zostavax (Stier *et al*, 2012). Given the lack of data it would be appropriate to leave a four week interval between administration of Yellow Fever vaccine and Zostavax.

In line with JCVI advice (JCVI February 2014), there are no other restrictions for timing between zostavax and other live vaccines.

Concurrent administration of Zostavax® and anti-viral medications known to be effective against VZV has not been evaluated, but drugs such as aciclovir are likely to reduce replication of the vaccine virus and therefore attenuate response. Therefore, Zostavax should not be administered to patients currently receiving oral or intravenous antiviral agents such as aciclovir or who are within 48 hours after cessation of treatment as the therapy may reduce the response to the vaccine.

Disposal (also refer to Chapter 3)

Equipment used for vaccination, including used vials, ampoules, or partially discharged vaccines should be disposed of at the end of a session by sealing in a proper, puncture-resistant 'sharps' box according to local authority regulations and guidance in the technical memorandum 07-01 (Department of Health, 2006).

Recommendations for the use of the vaccines

The aim of the national shingles immunisation programme is to lower the incidence and severity of shingles in older people. It is recommended that it be routinely offered to people aged 70 years.

A catch-up programme is also being rolled out in those aged 70-79 years, based on evidence of cost effectiveness and as this age group is likely to have the greatest benefit from vaccination (van Hoek *et al*., 2009). The reasons for this include:

- the burden of shingles disease within this age group (which increases with age),
- the estimated effectiveness of the vaccine within this age group (which decreases with age),
- the duration of protection of the vaccine, and
- the lack of knowledge about the effectiveness of a second dose of vaccine.

The course consists of a single dose of Zostavax®.

As Zostavax® can be administered concomitantly with inactivated influenza vaccine, the appointment for administration of the seasonal influenza vaccine is an appropriate opportunity to also provide Zostavax®, although any opportunity to provide the vaccine should be used.

Whilst the vaccine is authorised for use from age 50 years and is effective in this age group, the burden of shingles disease is generally not as severe in those aged 50-69 years when compared with older ages. Furthermore, given that the duration of protection is not known to last for more than ten years and the need for a second dose is not known, the vaccine is not recommended to be offered routinely below 70 years of age. Administration after 80 years of age is less cost-effective due to the limited effectiveness of the vaccine in older individuals.

Zostavax is not indicated for prevention of primary VZV infection (chickenpox) and should not be used in children and adolescents.

Management of at risk individuals following significant exposure to herpes zoster

Transmission of VZV can occur following direct contact with herpes zoster lesions, resulting in chickenpox in contacts who are susceptible to VZV. Therefore individuals at high risk of severe complications from varicella

infection should be assessed for the need for post exposure management with varicella zoster immunoglobulin (see **Chapter 34** for further details).

Zostavax® is not recommended for use as post-exposure prophylaxis or as a treatment for chickenpox or shingles.

Contraindications

The decision to administer Zostavax® to immunosuppressed individuals should be based on a clinical risk assessment. If the individual is under highly specialist care, and it is not possible to obtain full information on that individual's treatment history, then vaccination should not proceed until the advice of the specialist or a local immunologist has been sought.

Specialists with responsibility for patients in the vaccine eligible cohorts should include a statement of their opinion on the patient's suitability for Zostavax® in their correspondence with primary care. If primary healthcare professionals administering the vaccine have concerns about the nature of therapies (including biologicals) or the degree of immunosuppression they should contact the relevant specialist for advice.

The vaccine should not be given to a person who:

1. **Has primary or acquired immunodeficiency states** due to conditions including:
   - acute and chronic leukaemias, lymphoma (including Hodgkin's lymphoma)
   - immunosuppression due to HIV/AIDS (see later)
   - cellular immune deficiencies
   - those remaining under follow up for a chronic lymphoproliferative disorder including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma and other plasma cell dyscrasias (N.B: this list not exhaustive)
   - those who have received an allogenic stem cell transplant (cells from a donor) in the past 24 months and **only** then if they are demonstrated not to have ongoing immunosuppression or graft versus host disease(GVHD).
   - those who have received an autologous (using their own stem cells) haematopoietic stem cell transplant in the past 24 months and **only** then if they are in remission

Humoral deficiencies affecting IgG or IgA antibodies are not of themselves a contra-indication unless associated with T cell deficiencies. If there is any doubt (e.g. common variable immune deficiency), immunological advice should be sought prior to administration.

2. **Is on immunosuppressive or immunomodulating therapy** including:
   - those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for malignant disease or non-malignant disorders
   - those who are receiving or have received in the past 6 months immunosuppressive therapy for a solid organ transplant (depending upon the type of transplant and the immune status of the patient).
   - those who are receiving or have received in the past 12 months biological therapy (e.g. anti-TNF therapy such as alemtuzumab, ofatumumab and rituximab) unless otherwise directed by a specialist
   - those who are receiving or have received in the past 3 months immunosuppressive therapy including
     i) short term high-dose corticosteroids (>40mg prednisolone per day for more than 1 week);
     ii) long term lower dose corticosteroids (>20mg prednisolone per day for more than 14 days)
     iii) non-biological oral immune modulating drugs e.g. methotrexate >25mg per week, azathioprine >3.0mg/kg/day or 6-mercaptopurine >1.5mg/kg/day

Many adults with chronic inflammatory diseases (e.g. rheumatoid arthritis, inflammatory bowel disease, psoriasis, glomerulonephritis) may be on stable long term low dose corticosteroid therapy (defined as ≤20mg prednisolone per day for more than 14 days) either alone or in combination with other immunosuppressive drugs including biological and non-biological therapies. Long term stable low dose corticosteroid therapy (defined as ≤20mg prednisolone per day for more than 14 days) either alone or in combination with low dose non-biological oral immune modulating drugs (e.g. methotrexate ≤25mg per week, azathioprine ≤3.0mg/kg/day or 6-mercaptopurine ≤1.5mg/kg/day) are not considered sufficiently immunosuppressive and these patients can receive the vaccine. Specialist advice should be sought for other treatment regimes.

Zostavax® is **not** contraindicated for use in individuals who are receiving topical/inhaled corticosteroids or corticosteroid replacement therapy.

3. **Has had a confirmed anaphylactic reaction** to a previous dose of varicella – containing vaccine or any component of the vaccine, including neomycin or gelatin
4. **Is pregnant**
   Zostavax® is not indicated in women of childbearing age. Women who are pregnant should not receive Zostavax®.

Special considerations for the vaccination of individuals on immunosuppressive therapy

Patients anticipating immunosuppressive therapy

The risk and severity of shingles is considerably higher amongst immunosuppressed individuals and therefore eligible individuals anticipating immunosuppressive therapy should ideally be assessed for vaccine eligibility **before** starting treatment that may contra-indicate future vaccination.

Eligible individuals who have not received Zostavax® should receive a single dose of vaccine at the earliest opportunity and at least 14 days before starting immunosuppressive therapy, although leaving one month would be preferable if a delay is possible.

Precautions

Immunisation of individuals who are acutely unwell should be postponed until they have recovered fully. This is to avoid confusing the diagnosis of any acute illness by wrongly attributing any sign or symptoms to the adverse effects of the vaccine.

Immunisation should be delayed in individuals who are being treated with either oral or intravenous antivirals (such as aciclovir) until 48 hours after cessation of treatment. This is due to the potential to lower effectiveness of the vaccine as the therapy may reduce response to the vaccine. The use of topical aciclovir is not a contraindication to vaccination.

Zostavax® is not recommended for the treatment of shingles or post herpetic neuralgia (PHN). Individuals who have shingles or PHN should wait until symptoms have ceased before being considered for shingles immunisation. The natural boosting that occurs following an episode of shingles, however, makes the benefit of offering zoster vaccine immediately following recovery limited.

In immunocompetent individuals who develop shingles, vaccination should be delayed for one year. Patients who have two or more episodes of shingles in one year should have immunological investigation prior to vaccination. Clinicians may wish to discuss such cases with local specialist teams.

Further information on contraindications and special considerations for vaccination can be found in Chapter 6.

Immunosuppression and HIV infection

The decision to administer Zostavax® to immunosuppressed individuals should be based on clinical risk assessment (see above).

The safety and efficacy of Zostavax® have not been conclusively established in adults who are known to be infected with HIV with or without evidence of immunosuppression (see contraindications). On basis of limited Phase II trial data (Benson et al) and extrapolation from other live vaccines (Koenig et al [review]), a CD4 count of 200 cells/µl may be a suitable cut off value below which vaccination should not be given. Immunosuppressed patients who require protection against shingles should seek advice from a specialist.

Transmission

Post-marketing experience with varicella vaccines suggests that transmission of vaccine virus may occur rarely between those vaccinated who develop a varicella-like rash and susceptible contacts, although there has been no evidence of transmission of vaccine virus between vaccinees and susceptible contacts in the pre-licensure clinical trials of Zostavax®.

As a precautionary measure, any person who develops a vesicular rash after receiving Zostavax® should ensure the rash area is kept covered when in contact with a susceptible (chickenpox naïve) person until the rash is dry and crusted. If the person who received the vaccine is themselves immunosuppressed, they should avoid contact with susceptible people until the rash is dry and crusted, due to the higher risk of virus shedding. Prophylactic aciclovir can be considered in vulnerable patients exposed to a varicella like rash in a recent vaccinee.

Testing of post-vaccination rashes

In the event of a person developing a varicella (widespread) or shingles-like (dermatomal) rash post-Zostavax®, a vesicle fluid sample should also be sent for analysis to confirm the diagnosis and determine whether the rash is vaccine associated or wild type. This service is available at the Virus Reference

Department (VRD) at Public Health England, Colindale (T: 0208 327 6266). Please note sampling kits are not supplied by the Virus Reference Department at Public Health England. Health professionals are requested to obtain vesicle swabs from their local hospital laboratories. Forms and instructions on how to take a vesicle fluid sample can be found at: **https://www.gov.uk/government/publications/varicella-zoster-virus-referral-form**

Contact tracing is not required if an immunocompetent person develops a localised vesicular rash following vaccination.

Inadvertent vaccination in individuals under 50 years of age

Zostavax® is licensed for use in individuals over 50 years of age. However, most adults below the age of 50 years are likely to be immune to varicella and therefore inadvertent vaccination with Zostavax® is unlikely to result in serious adverse reactions. Based on limited data from two clinical trials including VZV-seronegative or low seropositive adults aged 30 years and older, the rates of local and systemic reactions were similar to those reported by other subjects who received the vaccine as part of a clinical trial. No serious vaccine related reactions were reported.

Although Zostavax® is similar to the varicella vaccine, it has a significantly higher antigen content. Early trials of varicella vaccine in susceptible children used doses of virus approaching the range used in Zostavax® (Weibel *et al*., 1984). The high dose formulation was well tolerated and efficacious. Inadvertent vaccination with Zostavax® in varicella naïve children is unlikely to result in serious adverse reactions and should count as a valid dose of varicella vaccine.

Inadvertent vaccination in immunosuppressed individuals

Immunosuppressed individuals who are inadvertently vaccinated with Zostavax® should be urgently assessed to establish the degree of immunosuppression. As all individuals of this age group should be VZV antibody positive, varicella-zoster immunoglobulin is unlikely to be of benefit but prophylactic aciclovir may be considered in those for whom the attenuated vaccine virus poses a significant risk. Immunosuppressed individuals who develop a varicella rash following inadvertent vaccination should be urgently assessed and offered prompt treatment with IV high-dose aciclovir, given the risks and severity of disseminated zoster.

Inadvertent vaccination during pregnancy

As a precautionary measure, clinicians should treat the inadvertent administration of Zostavax vaccine in a pregnant woman in the same way as a natural exposure to chickenpox infection and should urgently assess the woman's susceptibility to chickenpox.

For those women who are unable to give a reliable history of chickenpox infection or documented evidence of varicella vaccination, an urgent varicella antibody test (VZV IgG) should be performed. For those women who are found to be VZV IgG negative on testing, please contact the duty doctor at Public Health England (PHE) Colindale (T: 020 8200 4400) for further advice and consideration of the use of VZIG within 10 days of inadvertent vaccination. Ideally, VZIG should be administered within 7 days where practically possible but can be offered up to 10 days following vaccination. Samples from those pregnant women found to be VZV IgG negative on local testing will be requested to be sent to the Virus Reference Department for storage.

All incidents of inadvertent administration of Zostavax during pregnancy should also be reported to Public Health England using the vaccine administered in pregnancy reporting form (ViP). **https://www.gov.uk/vaccination-in-pregnancy-vip**

Adverse reactions

The safety of Zostavax® has been extensively evaluated in clinical trials; the most commonly reported side effects for Zostavax®, occurring in at least one in ten people, were injection site reactions including erythema (redness), pain, swelling, and pruritis (itching). Other common reactions reported in at least one in 100 people were haematoma, induration and warmth at the injection site, pain in arm or leg and headache. Very rarely, a varicella (chickenpox) like-illness was reported, in fewer than one in 10,000 people.

A full list of side effects can be found in the Zostavax® summary of product characteristics. (**https://www.medicines.org.uk/emc/medicine/25927**).

Serious suspected adverse reactions to Zostavax® should be reported to the Medical and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme (**www.mhra.gov.uk/yellowcard**).

Supplies

Zostavax® vaccine is manufactured by Merck & Co. Inc., USA – one of the parent companies of Sanofi Pasteur MSD (Tel: 0800 085 5511).

In England, this vaccine should be ordered online via the ImmForm website (**www.immform.dh.gov.uk**) and it is distributed by Movianto UK (Tel: 01234 248631) as part of the national immunisation programme. Further information about ImmForm is available at **http://immunisation.dh.gov.uk/immform helpsheets/** or from the ImmForm helpdesk at **helpdesk@immform.org.uk** or Tel: 0844 376 0040

Centrally purchased vaccines for the national immunisation programme for the NHS can only be ordered via ImmForm and are provided free of charge to NHS organisations. Vaccines for private prescriptions, outbreaks, occupational health use or travel are NOT provided free of charge and should be ordered from the manufacturers.

To obtain supplies of Zostavax® for use outside of the routine programme contact Sanofi Pasteur MSD, direct on Tel: 0800 085 5511.

In Northern Ireland, supplies of Zostavax® for the national immunisation programme are ordered from and distributed by Movianto N.I. (Tel: 028 9079 5799 Fax: 028 9079 6303)

In Scotland, supplies should be obtained from local vaccine-holding centres. Details of these are available from National Procurement (Tel. 0131 275 7587)

References

American Academy of Pediatrics (2006) Active Immunization. In: Pickering LK (ed.) *Red Book: 2006. Report of the Committee on Infectious Diseases. 27th edition.* Elk Grove Village, IL: American Academy of Pediatrics, pp. 9-54.

Banz K, Wagenpfeil S, Neiss A *et al.* (2003) The cost-effectiveness of routine childhood varicella vaccination in Germany. *Vaccine* **7**;21(11-12):1256-67.

Benson C, Hua L, Andersen J, *et al.* (2012) ZOSTAVAX is generally safe and immunogenic in HIV+ adults virologically suppressed on ART: results of a phase 2, randomized, double-blind, placebo-controlled trial. *Program and abstracts of the 19th Conference on Retroviruses and Opportunistic Infections; March 5-8, 2012; Seattle, Washington. Abstract 96*

Brisson M, Edmunds WJ, Law B *et al.* (2001) Epidemiology of varicella zoster virus infection in Canada and the United Kingdom. *Epidemiol Infect.* **127**(2):305-14.

Bowsher D (1999) The lifetime occurrence of Herpes zoster and prevalence of post-herpetic neuralgia: a retrospective survey in an elderly population. *Eur J Pain* **3**(4): 335-42.

Department of Health (2006) *Health Technical Memorandum 07-01: Safe Management of Healthcare Waste.* http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_063274 Accessed: April 2015.

Fleming DM (1999) Weekly Returns Service of the Royal College of General Practitioners. *Commun Dis Public Health* **2**(2): 96-100.

Gauthier A, Breuer J, Carrington D *et al.* (2009) Epidemiology and cost of herpes zoster and post-herpetic neuralgia in the United Kingdom. *Epidemiol Infect* **137**(1): 38-47.

Gilden DH, Dueland AN, Cohrs R *et al.* (1991) Preherpetic neuralgia. *Neurology.* **41**(8):1215-8.

Gnann JW and Whitley RJ (1991) Natural history and treatment of varicella-zoster virus in high-risk populations. *J Hosp Infect* **18**:317–29.

Harpez R, Ortega-Sanchez IR, Seward JF (2008) Prevention of Herpes Zoster, Recommendations of the Advisory Committee on Immunization Practices. *MMWR* **57** (RR-5)

Heymann AD, Chodick G, Karpati T, *et al* (2008). Diabetes as a risk factor for herpes zoster infection: results of a population-based study in Israel. *Infection*;**36**:226–230.

Katz J, Cooper EM, Walther RR *et al.* (2004) Acute pain in herpes zoster and its impact on health-related quality of life. *Clin Infect Dis* **39**:342-8.

Koenig HC, Garland JM, Weissman D, Mounzer K. (2013).Vaccinating HIV patients: focus on human papillomavirus and herpes zoster vaccines. *AIDS Rev.* Apr-Jun;15(2):77-86

Levin MJ, Oxman MN, Zhang JH *et al.* (2008) Varicella-zoster virus-specific immune responses in elderly recipients of a herpes zoster vaccine. *J Infect Dis* **197**(6): 825-35.

McCormick A, Charlton J and Fleming D (1995) Assessing health needs in primary care. Morbidity study from general practice provides another source of information. *BMJ* **310**(6993): 1534.

Miller E, Marshall R and Vurdien J (1993) Epidemiology, outcome and control of varicella-zoster infection. *Rev Med Microbiol* **4**(4): 222-30.

Mullooly J and Black S (2001) Simultaneous administration of varicella vaccine and other recommended childhood vaccines – United States, 1995–9. *MMWR* **50**(47): 1058-61.

Nagasawa K, Yamauchi Y, Tada Y *et al.* (1990) High incidence of herpes zoster in patients with systemic lupus erythematosus: an immunological analysis. *Ann Rheumatic Dis* **49**:630–3.

Opstelten W, Mauritz JW, de Wit NJ *et al*. (2002) Herpes zoster and postherpetic neuralgia: incidence and risk indicators using a general practice research database. *Fam Pract* **19**(5): 471-5.

Oxman MN and Levin MJ (2008) Vaccination against Herpes Zoster and Postherpetic Neuralgia. *J Infect Dis* **197** Suppl 2 S228-36.

Oxman MN, Levin MJ, Johnson GR *et al*. (2005) A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* **352**(22): 2271-84.

Pavan Langston D (1995) Herpes zoster ophthalmicus. *Neurology* **45**:50–1.

Ragozzino MW, Melton LJ, Kurland LT *et al*. (1982) Population-based study of herpes zoster and its sequelae. *Medicine* **61**:310--6.

Rogers SY, Irving W, Harris A *et al*. (1995). Visceral varicella zoster infection after bone marrow transplantation without skin involvement and the use of PCR for diagnosis. *Bone Marrow Transplant* **15**:805–7.

Schmader KE, Oxman MN, Levin MJ, Johnson G, Zhang JH, Betts R, Morrison VA, Gelb L, Guatelli JC, Harbecke R, Pachucki C, Keay S, Menzies B, Griffin MR, Kauffman C, Marques A, Toney J, Keller PM, Li X, Chan IS, Annunziato P; Shingles Prevention Study Group.(2012) Persistence of the efficacy of zoster vaccine in the shingles prevention study and the short-term persistence substudy *Clin Infect Dis*. Nov **15**;55(10):1320-8. doi: 10.1093/cid/cis638. Epub 2012 Jul 24.

Shaikh S, Ta CN (2002) Evaluation and management of herpes zoster ophthalmicus. *Am Fam Physician* **66**:1723–30.

Smitten AL, Choi HK, Hochberg MC *et al*. (2007) The risk of herpes zoster in patients with rheumatoid arthritis in the United States and the United Kingdom. *Arthritis Rheum* **57**:1431–8.

Stier DM, Weber IB, Staples JE. Lack of Interference by Zoster Vaccine With the Immune Response to Yellow Fever Vaccine. J Travel Med 2012; 19: 122–123.

Tseng HF, Smith N, Sy LS and Jacobsen SJ(2011) Evaluation of the incidence of herpes zoster after concomitant administration of zoster vaccine and polysaccharide pneumococcal vaccine. *Vaccine* **29**(20):3628-32

van Hoek AJ, Gay N, Melegaro A *et al*. (2009) Estimating the cost-effectiveness of vaccination against herpes zoster in England and Wales. *Vaccine* **27**(9): 1454-67.

Weibel RE, Neff BJ, Kuter BJ *et al*. (1984). Live attenuated varicella virus vaccine. Efficacy trial in healthy children. *N Eng J Med* **310**: 1409-15.

Wung PK, Holbrook JT, Hoffman GS *et al*. (2005) Herpes zoster in immunocompromised patients: incidence, timing, and risk factors. *Am J Med* **118**:1416.e9–e18.

Zostavax SPC Zostavax®: Summary of Product Characteristics. **https://www.medicines.org.uk/emc/medicine/25927** Accessed: April 2015.