

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

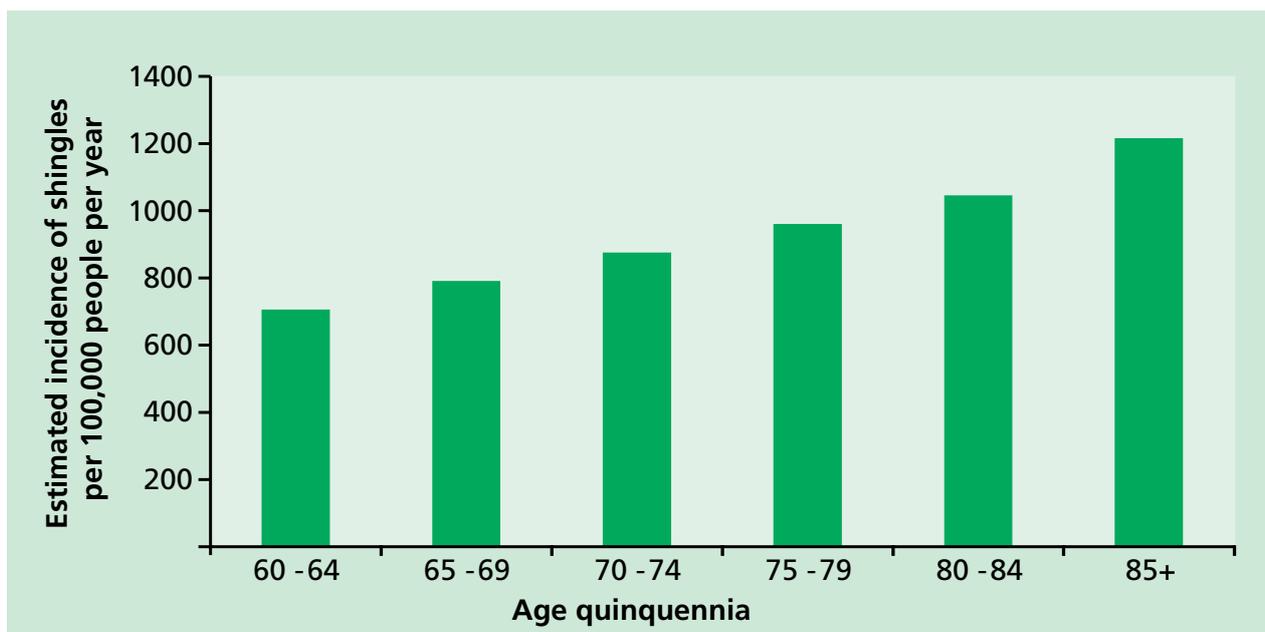


Figure 1 Estimated annual age-specific incidence of shingles per 100,000 per year in the immunocompetent population in England and Wales (population 2007). Data taken from van Hoek *et al.*, 2009.

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%

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

There are two licensed shingles vaccines available in the UK.

### Zostavax®

Zostavax® 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 the first three years of the UK vaccine programme with Zostavax®, vaccine effectiveness was 64% (95% CI 60-68%) against incident zoster and 81% (95% CI 61-91%) against PHN, with very similar VE estimates in the routine and catch-up cohorts (Walker *et al.* 2018).

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 occurs 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. In the first formal assessment of vaccine effectiveness

of the UK vaccine programme, there was evidence of waning VE over time, from 69% (95% CI 65-74%) in the first year after vaccination to 45% (95% CI 29-57%) by the third year.

In the first five years of the routine programme in England, an estimated 40,500 GP consultations and 1840 hospitalisations were averted through vaccination with Zostavax® (Andrews *et al*, 2020). These reductions were consistent with effectiveness in the routine cohorts (vaccinated aged 70) of between 37% (for hospitalised zoster) and 75% (for PHN consultations) and, in catch up cohorts (vaccinated aged 78 to 79) of between 49% (for hospitalised PHN) and 66% (for PHN consultations). Revaccination with Zostavax® is not recommended.

### **Shingrix®**

Shingrix® is a recombinant vaccine and contains varicella zoster virus glycoprotein E antigen produced by recombinant DNA technology, adjuvanted with AS01<sub>B</sub>.

In the phase 3 randomized placebo controlled clinical trials of 15,411 participants, vaccine efficacy in the 7,695 immunocompetent adults ≥ 50 years and 6,950 ≥70 years, administered with two doses of Shingrix® 2 months apart was estimated at 97.2% and 91.2% respectively (Lal *et al* 2015),

In a phase 3 clinical trial in autologous haemopoietic stem cell transplant recipients aged 18 years and above who received two doses of Shingrix® 1-2 months apart, robust humoral and cellular responses persisted at 1 year after vaccination. (Dagnew *et al*, 2019) Post hoc efficacy analysis revealed a vaccine efficacy of 87.2% against herpes zoster in immunocompromised patients which included non-Hodgkin B-cell lymphoma and chronic lymphocytic leukaemia.

One and two dose real world vaccine effectiveness of Shingrix® was estimated at 56.9% and 70.1% respectively in a US study of adults aged >65 years (Izurieta *et al*, 2021). Two-dose vaccine effectiveness against postherpetic neuralgia was 76.0% (95% CI, 68.4-81.8). The two-dose vaccine effectiveness was not significantly lower for adults 80+ years, for second doses received at ≥180 days, or for individuals with autoimmune conditions.

### **Storage**

#### **Zostavax® and Shingrix®**

The unreconstituted vaccines and their diluents 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®**

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.

### Shingrix®

Shingrix® is available as a white powder for reconstitution with diluent and is injected as a suspension. After reconstitution, the suspension is an opalescent colourless to pale brownish liquid.

Shingrix® is available in a pack size of 1 vial of powder plus 1 vial of suspension or in a pack size of 10 vials of powder plus 10 vials of suspension. The reconstituted vaccine should be inspected visually for any foreign particulate matter and/or variation of appearance. If either is observed, the vaccine should not be administered.

After reconstitution, the vaccine should be used promptly; if this is not possible, the vaccine should be stored in a refrigerator (2°C – 8°C). If not used within 6 hours it should be discarded.

### Dosage and schedule

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

Adults should receive two doses of **0.5ml** of Shingrix® a minimum of 2 months apart.

### 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. For individuals with a bleeding disorder, Zostavax® should be given by deep subcutaneous injection to reduce the risk of bleeding.

Shingrix® should be given by intramuscular injection, preferably in the deltoid region of upper arm. Subcutaneous administration is not recommended. Shingrix® should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration to these subjects. The vaccines must not be given intravascularly. Further information on injection technique can be found in [Chapter 4](#).

Where Zostavax® or Shingrix® vaccine is given at the same time as another vaccine, 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.

### 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 arrangements and guidance in the Health Technical Memorandum 07-01: Safe management of healthcare waste (Department of Health, 2013).

## 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.

Two vaccines are licensed and available in the UK; Zostavax® (a live vaccine) which is given as a single dose and Shingrix® (recombinant sub-unit vaccine) which is given as a two-dose schedule.

### National programme for adults aged 70-79 years

The routine programme for people aged 70 years, using Zostavax®, has been in place since 2013. At the same time a catch-up programme was rolled out to those aged 70-79 years in a phased approach. The choice of age group was based on evidence of cost effectiveness of Zostavax®. This age group are likely to have the greatest ability to benefit from vaccination (van Hoek *et al.*, 2009) for the following reasons:

- the burden of shingles disease within this age group (which increases with age)
- the estimated effectiveness of Zostavax® within this age group (which decreases with age)
- the duration of protection of Zostavax®, and
- the limited data on the effectiveness of a second dose of Zostavax® vaccine

The course consists of a single dose of Zostavax®

Whilst Zostavax® 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 duration of protection wanes over time the vaccine is not recommended to be offered routinely below 70 years of age. Administration after 80 years of age is also less cost-effective due to the lower effectiveness of the vaccine in older individuals.

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

### Immunosuppressed individuals aged 70 to 79 years

From 2021, individuals who are eligible for shingles vaccine (adults aged 70-79 years), but who are contra-indicated to the receipt of the live vaccine should be offered Shingrix® instead. Individuals who should be offered Shingrix® instead of Zostavax® amongst this age group are summarized below (Box). If there is any doubt, individual patients should be discussed with their specialist.

Supply of Shingrix® is currently limited and so individuals aged 70-79 years with lower levels of immunosuppression should be offered Zostavax®. Primary humoral immunodeficiencies such as X-linked agammaglobulinemia, are not of themselves an indication for Shingrix® unless associated with T cell defects. If there is any doubt, specialist advice from an immunologist should be sought. Individuals who received high dose short term immunosuppression at doses equivalent to  $\leq 40$ mg prednisolone per day for an acute episode of illness such as asthma / chronic obstructive pulmonary disease (COPD) or COVID-19 are not considered severely immunosuppressed and may be vaccinated with Zostavax® when they have recovered.

Shingrix® should not be offered to those on replacement corticosteroids for adrenal insufficiency, or to those topical or inhaled corticosteroids or corticosteroid replacement therapy, who can receive Zostavax® instead.

**Box: Definition of severe immunosuppression****Individuals with primary or acquired immunodeficiency states due to conditions including:**

- acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who are less than 12 months since achieving cure
- individuals under follow up for a chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (N.B: this list not exhaustive)
- immunosuppression due to HIV/AIDS with a current CD4 count of below 200 cells/ $\mu$ l.
- primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ $\mu$ l) or with a functional lymphocyte disorder
- those who have received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months
- those who have received a stem cell transplant more than 24 months ago but have ongoing immunosuppression or graft versus host disease (GVHD)

**Individuals on immunosuppressive or immunomodulating therapy including:**

- those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for any indication
- those who are receiving or have received in the previous 6 months immunosuppressive therapy for a solid organ transplant
- those who are receiving or have received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but for which a 6 month period should be considered immunosuppressive), monoclonal tumor necrosis factor inhibitors (TNFi), T-cell co-stimulation modulators, soluble TNF receptors, interleukin (IL)-6 receptor inhibitors., IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (N.B: this list is not exhaustive)

**Individuals with chronic immune mediated inflammatory disease who are receiving or have received immunosuppressive therapy**

- moderate to high dose corticosteroids (equivalent  $\geq$ 20mg prednisolone per day) for more than 10 days in the previous month
- long term moderate dose corticosteroids (equivalent to  $\geq$ 10mg prednisolone per day for more than 4 weeks) in the previous 3 months
- any non-biological oral immune modulating drugs e.g. methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day; 6-mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day) in the previous 3 months
- certain combination therapies at individual doses lower than stated above, including those on  $\geq$ 7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months

**Individuals who have received a short course of high dose steroids (equivalent >40mg prednisolone per day for more than a week) for any reason in the previous month.**

## Reinforcing immunisation

The need for booster doses of either Shingrix® and Zostavax® has not yet been determined.

## Co-administration with other vaccines

Zostavax® can be given at the same time as inactivated influenza vaccination. Therefore, an appointment for administration of the seasonal influenza vaccine can be an opportunity to also provide Zostavax® although the vaccine should be offered all year round, rather than purely as a seasonal programme. 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, if Zostavax® is being used.

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, an 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).

In phase III controlled open label clinical studies of Shingrix® in adults aged 50 years and older, individuals received either concomitant unadjuvanted inactivated seasonal influenza vaccine or PPV-23 with their first dose of Shingrix®. The immune responses of the co-administered vaccines were unaffected, although fever and shivering were more commonly reported when PPV-23 was given with Shingrix®.

Shingrix® can be given concomitantly with inactivated influenza vaccine. Because of the absence of data on co-administration of Shingrix® vaccine with adjuvanted influenza vaccine, it should not be routine to offer appointments to give this vaccine at the same time as the adjuvanted influenza vaccine. Based on current information, scheduling should ideally be separated by an interval of at least 7 days to avoid incorrect attribution of potential adverse events. Where individuals attend requiring both vaccines, however, and require rapid protection or are considered likely to be lost to follow up, co-administration may still be considered.

Immunisation with Zostavax® and Shingrix® should ideally be delayed for seven days after COVID-19 vaccination and vice versa. Neither vaccine has been tested for routine co-administration; there is potential for the side effects of Shingrix® to be confused with those of COVID-19 vaccines, and there may be a reduced response to Zostavax®. Where individuals attend requiring both vaccines, however, and require rapid protection or are considered likely to be lost to follow up, co-administration may still be considered.

Based on evidence that MMR vaccine can lead to an attenuation of the response to varicella vaccine (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.

As Shingrix® is an inactivated vaccine, where individuals in an eligible cohort present having received another inactivated or live vaccine, Shingrix® vaccination should still be considered. In most cases, vaccination should proceed to avoid any further delay in protection and to avoid the risk of the patient not returning for a later appointment. In such circumstances, patients should be informed about the likely timing of potential adverse events relating to each vaccine.

### Previous incomplete vaccination

If the course of Shingrix® is interrupted or delayed, it should be resumed using the same vaccine but the first dose should not be repeated.

### Pregnancy

Zostavax® is not indicated in women of childbearing age. Women who are pregnant should not receive Zostavax®.

There is no known risk associated with giving inactivated, recombinant viral or bacterial vaccines or toxoids during pregnancy or whilst breast-feeding (Kroger *et al.*, 2013). If indicated, Shingrix® can be considered in pregnancy after full discussion of the risks and benefits of vaccination with the woman

### Contraindications

#### Shingrix®

Shingrix® should not be administered to an individual with a confirmed anaphylactic reaction to any component of the vaccine.

#### Zostavax®

Zostavax® should not be given to an individual who has had a confirmed anaphylactic reaction to a previous dose of varicella virus – containing vaccine or to any component of the vaccine.

Zostavax® is not indicated in women of childbearing age. Women who are pregnant should not receive Zostavax®.

Zostavax® is also contraindicated in those with severe immunosuppression ([see box page 7](#)).

Primary humoral immunodeficiencies, such as X-linked agammaglobulinemia, are not of themselves a contra-indication for Zostavax® unless associated with T cell defects.

Immunosuppression at doses equivalent to  $\leq 40$ mg prednisolone per day for an acute episode of illness such as asthma, chronic obstructive pulmonary disease (COPD) or COVID-19 may be vaccinated with Zostavax® when they have recovered. Zostavax® may also be offered to those on replacement corticosteroids for adrenal insufficiency, or to those topical or inhaled corticosteroids or corticosteroid replacement therapy.

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.

## Immunosuppression and HIV

Individuals aged 70-79 years with severe immunosuppression ([see box page 7](#)) should receive Shingrix® instead of Zostavax®. Individuals with lower levels of immunosuppression can receive Zostavax®. Specialists with responsibility for patients in the vaccine eligible cohorts who are immunosuppressed should include a statement of their opinion on the patient's suitability for Zostavax® in their correspondence with primary care.

### Individuals aged 70-79 years 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 Zostavax® vaccination. Supply of Shingrix® is currently limited and vaccine supplied via the national programme should not be used for pre-treatment vaccination. Eligible individuals who have not previously 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.

## 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 antivirals or varicella zoster immunoglobulin (see [Chapter 34](#) for further details).

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

### 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.

Zostavax® and Shingrix® are not recommended for the treatment of shingles or post herpetic neuralgia (PHN). Individuals who have shingles 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 unclear. 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.

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. Immunisation with Zostavax® should be delayed in individuals who are being treated for non-varicella zoster infections with either oral or intravenous antivirals (such as aciclovir) until 48 hours after cessation of treatment. This also applies to individuals receiving acyclovir prophylaxis which should be ceased for at least 48 hours before vaccination and individuals who have received high dose IVIG or varicella zoster immunoglobulin (VZIG) in the previous 6 weeks.

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 either Zostavax® or Shingrix® vaccination.

### Transmission after live vaccination

Post-marketing experience with live varicella vaccines (Varivax and Varilrix) suggests that transmission of vaccine virus may occur rarely between those vaccinated who develop a varicella-like rash and susceptible contacts, although there was 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.

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

As Shingrix® is a recombinant protein vaccine there are no risks of developing varicella-like rashes following administration of Shingrix®.

### Testing of post Zostavax® 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 6017). 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>

### Inadvertent vaccination with Zostavax® 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 of Zostavax® in immunosuppressed individuals

Immunosuppressed individuals who are inadvertently vaccinated with Zostavax® should be urgently assessed to establish the degree of immunosuppression. All individuals of this age group should be VZV antibody positive, and so, varicella-zoster immunoglobulin (VZIG) 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 with Zostavax® 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, treat as an exposure to chickenpox and assess the need for post-exposure treatment with antivirals or VZIG. 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>).

The safety of Shingrix® has been evaluated in clinical trials; in those aged 50 years and above the most frequently reported side effects were pain at the injection site (68%), myalgia (33%), and fatigue (32%). Most of these reactions were not long-lasting (median duration 2-3 days).

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

Shingrix® is manufactured by GlaxoSmithKline ; the marketing authorization holder is GlaxoSmithKline UK Limited (Tel: 0800 221 441).

In England, these vaccines should be ordered online via the ImmForm website ([www.immform.dh.gov.uk](http://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/](http://immunisation.dh.gov.uk/immform_helpsheets/) or from the ImmForm helpdesk at [helpdesk@immform.org.uk](mailto: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.

To obtain supplies of Shingrix® for use outside of the national immunisation programme contact GlaxoSmithKline UK, direct on Tel: 0800 221 441.

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)

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