23 Varicella-Zoster

VARICELLA HOSPITALISATION NOTIFIABLE
OUTBREAK NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the product Summary of Product Characteristics (SmPC). When this occurs, NIAC advises that the recommendations in these guidelines, which are based on current expert advice from NIAC, are followed.

Contents

Key changes

The chapter has been extensively revised October 2024.

The primary childhood immunisation and primary school programme schedule is changing for those born on or after 1st October 2024 with the introduction of varicella vaccination at 12 months of age and a second dose in Junior Infants.

NIAC recommends recombinant zoster vaccine (RZV, Shingrix) against herpes zoster (HZ) and no longer recommends vaccination with live zoster vaccine (ZVL, Zostavax).

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Introduction

Varicella-zoster virus (VZV) is one of eight herpes viruses known to cause human infection and is distributed worldwide. Two distinct clinical syndromes are associated with VZV infection - varicella (chickenpox) and herpes zoster (shingles).

Primary infection results in varicella, an acute exanthematous disease. Varicella is usually a mild disease. However, complications can occur, most often in infants, adults, pregnant women and the immunocompromised.

The virus becomes latent in the cells of the dorsal root or cranial nerve ganglia and may reactivate after a period, which may be several decades. Reactivation results in herpes zoster.

23.2 Epidemiology

VZV is very infectious; one case of primary varicella can infect 10-12 susceptible people (R0 10-12).

In Ireland, the incidence of varicella is seasonal, reaching a peak between January and April. Transmission is by inhalation of respiratory droplets, by direct contact with vesicular fluid, or by contact with fomites. VZV can be transmitted from individuals with zoster to non-immune contacts resulting in varicella. Such transmission is infrequent and is dependent on direct or indirect contact, including inhalation, from non-intact vesicles.

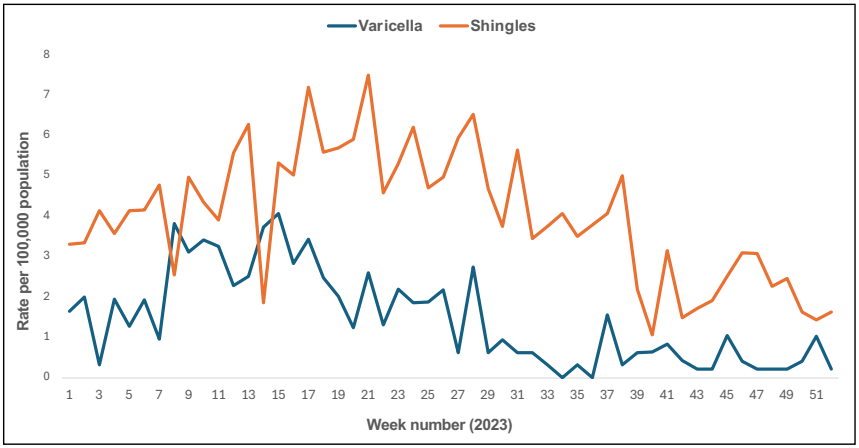
The incubation period is from 10 to 21 days; the majority develop disease between 14 and 16 days. The incubation period may be prolonged up to 28 days in immunocompromised patients and in individuals who have received varicella-zoster immunoglobulin (VZIG).

Cases of ***varicella*** are infectious from two days before the appearance of the rash until all of the lesions have crusted, typically a total of seven days. This may be prolonged in immunocompromised individuals. In the family setting, the secondary attack rate ranges from 60-90% for susceptible persons.

The period of infectivity of ***zoster*** is typically five days, from the appearance of the lesions until all lesions have crusted. Viral load and/or viral shedding may be increased with increased risk of transmission if the lesions are exposed or disseminated, or from immunocompromised patients with localised zoster on any part of the body.

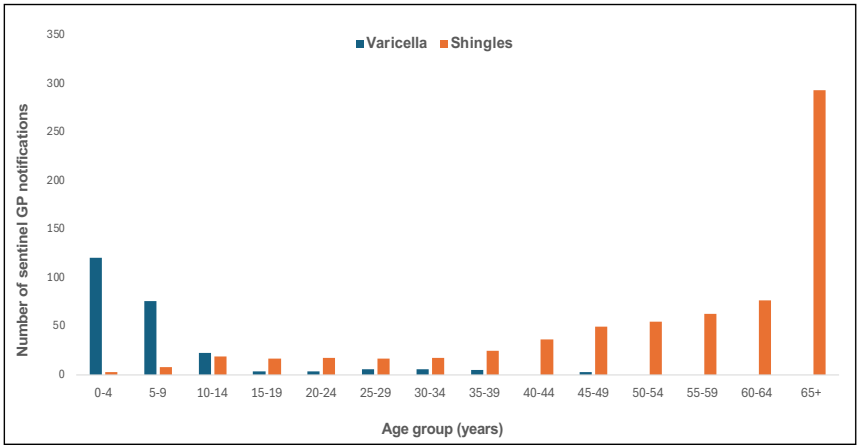
In Ireland, hospitalised cases of varicella became notifiable in 2011. In 2023, there were 165 varicella hospitalised cases notified and no reported deaths. These data likely considerably underestimate the true burden of this disease. Varicella and zoster incidence in the community is estimated from data obtained from the sentinel surveillance system of the Irish College of General Practitioners (ICGP)/ Health Protection Surveillance Centre (HPSC) (Figure 23.1).

Figure 23.1 Varicella and zoster rates per 100,000 population by week 2023
Source: ICGP/HPSC sentinel surveillance



In 2023, most notified varicella cases occurred in children aged under five years and most notified zoster cases occurred in those aged 65 years and older (Figure 23.2).

Figure 23.2. Varicella and zoster notifications from sentinel GP sites, 2023
Source: ICGP/HPSC sentinel surveillance



In the USA prior to the introduction of routine childhood varicella vaccination, adults had a 25 times greater risk and infants had a four times greater risk of dying from varicella than did children 1-4 years old. Since the introduction of varicella vaccine in the U.S. in 1995 the number of hospitalisations and deaths from varicella has decreased markedly.

23.3 Effects of varicella

Varicella is typically a benign infection of childhood characterised by a generalised pruritic vesicular rash. A mild prodrome of fever and malaise may occur, more commonly in adults. The rash usually starts on the head and progresses to the trunk and extremities. The rash may involve mucous membranes (mouth, respiratory tract, vagina, conjunctiva and cornea). The rash progresses from macules to papules to vesicular lesions that crust over as they dry. Successive crops appear over several days. The number of lesions ranges from a few to hundreds.

Varicella is highly contagious with a household attack rate of 90% for non-immune individuals who come into close contact. In children, the clinical course is generally mild with malaise, pruritus and fever for 2-3 days. Complications are uncommon in childhood and include superinfection (usually with Group A streptococcus), skin scarring, encephalitis, pneumonia, glomerulonephritis, myocarditis, hepatitis and coagulopathy. The risk of complications is higher in infants under one year of age and in those

aged 15 years and older, particularly pregnant women, smokers, and the immunocompromised.

Recovery from varicella usually results in lifelong immunity. Recurrent disease is rare but is more likely in immunocompromised individuals.

Diagnosis is primarily clinical and can be confirmed from a swab of vesicular fluid by PCR, culture or biopsy for electron microscopy. Serology is also available and can be used to demonstrate immunity.

23.3.1 Varicella infection during pregnancy

Varicella infection in non-immune pregnant women carries an increased risk of severe varicella pneumonia in the mother, especially late in the second and early in the third trimester. Risks to the fetus and neonate are related to the timing of maternal infection.

23.3.2 Congenital varicella syndrome

In a large prospective study of maternal varicella, the incidence of congenital varicella syndrome was <1% in the first 12 weeks of pregnancy, approximately 2% between 13 and 20 weeks, with no cases after 20 weeks' gestation.

Effects include limb hypoplasia, microcephaly, cataracts, growth restriction and skin scarring. Congenital varicella syndrome is associated with a mortality rate of 30% in the first few months of life.

Maternal varicella during pregnancy is also associated with the subsequent development of zoster during childhood. In a study published in 1994, ten children of 1,373 women with primary varicella during pregnancy developed childhood zoster.

Congenital varicella syndrome following maternal zoster is extremely rare.

23.3.3 Neonatal varicella

Varicella occurring in a mother within one week before and one week after delivery is associated with an increased risk of neonatal infection. The highest risk is associated with maternal infection from five days before to two days after delivery, with a mortality rate up to 30% in the infant. Postnatally acquired varicella that occurs 10 days or more after birth is typically mild. However, because of their relative immunologic immaturity, newborns are at greater risk for acquiring severe disease than are older infants or children.

23.3.4 Varicella in immunocompromised persons

Those at increased risk of severe complications include severely immunocompromised individuals, especially those who have leukaemia or other disorders in which there is depressed cell mediated immunity, solid organ transplant recipients on immunosuppressive treatment, and those with rheumatological diseases treated with tumour necrosis factor (TNF) antagonists (Chapter 3).

23.4 Effects of herpes zoster

Herpes zoster (shingles) is caused by the reactivation of latent varicella zoster virus (VZV) and usually occurs decades after primary infection. The individual lifetime risk of developing herpes zoster (HZ) is between 24% and 30%. Although zoster can occur at any age, incidence increases with older age. Two-thirds of cases occur in those aged 50 years and older. The risk of developing the disease in those aged ≥85 years is 50%. Children are more likely to develop zoster if infection with varicella occurred in utero or during infancy.

Immunocompromised individuals of any age are at increased risk of HZ. Risk varies depending on the underlying condition and immunocompromising treatment. Data on the incidence of HZ and its complications in immunocompromised individuals in Ireland are limited. In adult patients with immunocompromise the highest incidence of HZ occurs in haematologic stem cell transplant (HSCT) patients, followed in order of incidence by haematological malignancies (HM), solid organ transplant (SOT), solid organ malignancies (SOM) and human immunodeficiency virus (HIV).

The risk of HZ associated with these conditions is greater than the risk associated with older age in the immunocompetent. However, within patients with these conditions the risk of HZ increases with increasing age except in the case of HSCT and in those living with HIV prior to the introduction of antiretroviral therapy. For HSCT patients the risk is comparably high across age groups from 18 years old and above.

Although HSCT, haematological malignancy, solid organ transplant, solid organ malignancy and HIV patients are at the highest risk of HZ and its complications, patients with autoinflammatory and immunocompromising conditions such as rheumatoid arthritis and systemic lupus erythematosus have also been shown to be at increased risk. An increased risk has been

observed among patients receiving therapy with biologics especially those treated with TNF-α antagonists and patients who received high-dosage non-biologic disease-modifying antirheumatic drugs (nbDMARDS), Janus kinase inhibitors (JaKi) or high-dose corticosteroids.

Zoster is characterised by a vesicular rash localised in the sensory region of the affected ganglia and is often preceded or accompanied by acute pain or itching. Headache, photophobia, myalgia and malaise may occur in the prodromal phase, which lasts 1-10 days (average two days).

The rash most commonly appears on the trunk, in one or two thoracic dermatomes (*localised zoster*), not typically crossing the midline. Less commonly, the rash can affect three or more dermatomes (*disseminated zoster*). This generally occurs in the immunocompromised. Disseminated zoster can be difficult to distinguish from varicella.

Zoster of the trigeminal nerve should be considered in a patient with a prior history of varicella presenting with blurred vision and a painless red eye. Urgent ophthalmological opinion should be sought.

New vesicles continue to form over three to five days and progressively dry and crust. The rash usually resolves in two to four weeks; permanent pigmentation changes and scarring may occur in the skin over affected dermatomes.

Complications associated with HZ infection include post herpetic neuralgia (PHN), ocular complications, meningitis and herpes zoster oticus.

Pain associated with HZ, persisting or appearing more than 90 days after the onset of rash is a commonly accepted definition of postherpetic neuralgia (PHN). The pain can be severe and incapacitating and can persist for months and occasionally for years. Older adults are most likely to have PHN and to have longer lasting and more severe pain (over 13% of those aged 60 years and older with zoster will develop PHN).

Diagnosis is primarily clinical. Diagnosis can be confirmed from a swab of vesicular fluid by PCR, culture or biopsy for electron microscopy. Serology is also available and can be used to demonstrate immunity.

23.5 Varicella vaccines

Three varicella vaccines are licensed:

1. monocomponent VARIVAX
2. varicella in combination with measles, mumps and rubella vaccines (MMRV, ProQuad)
3. varicella in combination with measles, mumps and rubella vaccines (MMRV, Priorix-Tetra).

VAVIRAX is the only one of these three vaccines currently available for use in Ireland.

23.5.1 VARIVAX

Varicella vaccine (VARIVAX) is a live virus vaccine produced in human diploid cells.

Licensed indications

Active immunisation against varicella:

- in healthy individuals from the age of 12 months
- for post exposure prophylaxis if administered to healthy, susceptible individuals exposed to varicella within 72 hours of contact in individuals at high risk of severe varicella.

Storage

As the vaccine is less stable than other live virus vaccines, storage temperature requirements are critical to ensure optimum vaccine effectiveness. The unreconstituted vaccine and its diluent should be stored in the original packaging in a refrigerator at +2°C to +8°C and protected from light. Following reconstitution, the vaccine should be used immediately. Discard any unused reconstituted vaccine after 30 minutes.

Efficacy

Overall, two dose vaccine efficacy in younger children is between 86-98% and approximately 75% in adolescents and adults. Immunity appears to be long lasting in most individuals. Mild breakthrough infections may occur in a minority of recipients.

Dose, route of administration and schedule

The dose is 0.5 mls IM into the anterolateral thigh or the deltoid.

Age 12 months to 12 years: two doses at least four weeks apart. Those with asymptomatic HIV infection with an age-specific CD4+ count of ≥25% should receive two doses 12 weeks apart.

Age 13 years and older: two doses 4-8 weeks apart.

Contraindications

1. Anaphylaxis to any of the vaccine constituents.
2. Immunocompromise from disease or treatment (Chapter 3).
3. Active untreated tuberculosis.
4. Pregnancy.
5. Individuals with a family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential recipient is demonstrated.

Precautions

1. Acute severe febrile illness, defer until recovery.
2. Recent (3-11 months) receipt of an antibody-containing product (Chapter 2, Table 2.6).
3. Receipt of some antivirals (e.g. acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination.
4. Pregnancy should be avoided for four weeks following vaccination.
5. If not given at the same time as MMR vaccine, the vaccines should be separated by at least four weeks. The risk of breakthrough varicella is increased if varicella vaccine is administered less than four weeks following MMR vaccine.
6. Infants of breastfeeding mothers receiving monoclonal antibody treatment (including infliximab) post-partum should be immunised with varicella vaccines according to routine schedule. If there is any doubt as to whether an infant due to receive a live attenuated vaccine such as varicella vaccine may be immunosuppressed due to the mother's therapy, specialist advice should be sought.

The following are NOT contraindications

1. Pregnancy of recipient's mother or other close or household contact.* The benefits of protecting a non-immune pregnant household contact from exposure to varicella from a varicella vaccine related rash, by vaccinating her other children, far outweigh the small, theoretical, risk of transmission of vaccine virus to these individuals. Over a 10 year period in the USA, 55 million doses of varicella vaccine were distributed and transmission was documented from five people, resulting in six secondary cases of varicella. All six secondary cases were mild. No adverse effects have been documented on either pregnant women or fetuses.
2. Immunocompromised family member or household contact.* The risk to the immunocompromised person, should the child develop a varicella vaccine related rash, is negligible compared to the risk to the immunocompromised person, should the child develop varicella infection.
3. Treatment with low dose, alternate-day, topical, replacement, or aerosolised steroid preparations (Chapter 3). Low dose prednisolone or its equivalent for children weighing <10kg is <2mg/kg/day for less than two weeks. Low dose prednisolone or its equivalent for adults and children weighing ≥10kg is <20 mg/day for less than two weeks or <40 mg/day for less than or equal to one week (Chapter 3, Table 3.7).
4. Natural varicella infection and salicylate use have been associated with an increased risk of developing Reye's syndrome. However, there are no reports of an association between Reye's syndrome and varicella vaccination. People taking long-term salicylate therapy can receive varicella-containing vaccine, if needed. The benefit is likely to outweigh any possible risk of Reye's syndrome after varicella vaccination.
5. Asymptomatic or mildly symptomatic HIV infection (CD4 count ≥15%). (Chapter 3).
6. Humoral immunodeficiency (e.g. agammaglobulinemia).
7. Breastfeeding.

*If a vaccinee has a presumed vaccine related rash 7-25 days after vaccination, they should avoid direct contact with immunocompromised persons, non-immune pregnant women and their newborn in the first week of life, and non-immune infants in neonatal units, for the duration of the rash.

Coadministration
VAVIRAX may be given at the same time, but at a different injection site from a combined measles, mumps, and rubella (MMR) vaccine, Haemophilus influenzae type b conjugate vaccine, hepatitis B vaccine, diphtheria/tetanus/whole-cell pertussis vaccine, and oral polio virus vaccine.

MMR vaccine and monovalent varicella vaccine can be administered into the same limb, 2.5 cm apart. If a person receives MMR vaccine at the same time as monovalent varicella vaccine, separate syringes and injection sites should be used. MMR vaccine and monovalent varicella vaccine should not be mixed together before injection.

If varicella vaccine (live) (Oka/Merck strain) is not given concomitantly with measles, mumps, and rubella virus vaccine live, a four week interval between the two live virus vaccines should be observed.

Men B vaccine should be administered in a separate limb.

Adverse reactions
Common adverse events are listed below, a full list of adverse reactions may be found in the SmPC.

Local:	Common: pain, redness, tenderness, varicella-like rash (injection site, median two lesions).
General:	Very common: fever ≥38°C. Common: fever ≥39°C, irritability, upper respiratory infection, maculopapular rash, varicella-like rash (generalised, median five lesions).

Transmission of vaccine virus can occur, but the risk is very low and primarily occurs in the presence of a post-vaccination rash (see * on page 12).

23.6 Varicella vaccine recommendations

23.6.1 Routine childhood vaccination

The primary childhood immunisation and school immunisation programme schedule has changed for those born on or after 1st October 2024 with the introduction of varicella vaccination. Two doses of varicella vaccine are recommended.

The primary childhood immunisation and school immunisation programme schedule which has been in operation for all babies born on or after 1st October 2016 does not include routine childhood varicella vaccination.

From 1st October 2025, all children at 12 months of age should receive a monovalent varicella vaccine. They should receive an MMRV vaccine at 4-5 years of age. This MMRV vaccine replaces the MMR vaccine.

Infants who were infected with varicella under the age of 12 months should still receive two doses of varicella vaccine, due to the increased risk of a second episode of varicella infection. Previous varicella infection is not a contraindication to varicella vaccination. Children who have had varicella infection can receive varicella-containing vaccines.

Vaccination with MMRV is not contraindicated if a child who received the first dose of varicella vaccine at the age of 12 months has a breakthrough varicella infection. Children who have had varicella infection can receive MMRV, although it may be of limited additional benefit.

Vaccination may be considered for any non-immune persons aged 12 months or older. Those who choose to have themselves or their child immunised should consult with their GP.

23.6.2 Vaccination of children in risk groups

Two doses of varicella vaccine, at least four weeks apart, are recommended for **non-immune children** without a definite history of varicella, proof of immunity, or vaccination from 12 months of age in the following risk groups:

- Some immunocompromised patients, e.g. those with lymphocytic leukaemia in remission, and transplant recipients following immune reconstitution (Chapter 3, Table 3.9).
- Children in residential units with physical and intellectual disability. Those without a history of varicella should have their immunity checked.
- Close household contacts of immunocompromised patients.
- Some HIV infected children (Chapter 3, Table 3.5 and Table 3.6).

23.6.3 Vaccination of adults in risk groups

Two doses of varicella vaccine, at least four weeks apart, are recommended for **non-immune adults** without a definite history of varicella, proof of immunity, or vaccination from 12 months of age in the following risk groups:

- Some immunocompromised patients, e.g. those with lymphocytic leukaemia in remission, and transplant recipients following immune reconstitution (Chapter 3, Table 3.9).
- Close household contacts of immunocompromised patients.

- Non pregnant women of reproductive age. Those with negative serology should be vaccinated prior to or after pregnancy. Pregnancy should be avoided for four weeks following varicella vaccination.

23.6.4 Vaccination of healthcare workers (HCWs)

All HCWs who have direct patient contact both clinical and non-clinical should be immune to varicella (Chapter 4, Section 4.2.9).

Acceptable presumptive evidence of immunity against varicella includes at least one of the following:

- documented evidence of two doses of varicella vaccine given at least four weeks apart

or

- serological evidence of immunity (positive varicella IgG titre)

or

- definite clinical history of varicella infection. (A history of varicella may be a less reliable predictor of immunity in individuals born and raised overseas, and therefore routine testing should be considered in this group of HCWs).

Two doses of varicella vaccine at least four weeks apart, are recommended for non-immune HCWs without acceptable evidence of immunity.

Routine post vaccination serology is not recommended.

HCWs should consult the Occupational Health Department if they develop a post varicella vaccine rash. If a HCW develops a localised rash following varicella vaccination, the lesions should be covered and the HCW can continue patient contact. A risk assessment should be carried out if they are working with high-risk patients. If a HCW develops a generalised rash following varicella vaccination, the HCW should be excluded from patient contact until the lesions are crusted.

23.6.5 Vaccination of laboratory staff

Two doses of varicella vaccine, at least four weeks apart, are recommended for non-immune individuals without a definite history of varicella, proof of immunity, or vaccination from 12 months of age in the following risk group:

- laboratory staff exposed to varicella virus in the course of their work.

23.7 Herpes zoster vaccines

It is not necessary to determine whether patients have a history of varicella or zoster prior to vaccination because waning antibodies in previously exposed patients (particularly older adults) may lead to negative results despite past infection.

Zostavax (ZVL) is a live attenuated vaccine and Shingrix (RZV) is a non-live recombinant vaccine. Shingrix (RZV) is more effective than ZVL and unlike ZVL it can be safely administered to immunocompromised patients. Shingrix is the preferred vaccine against HZ due to its greater efficacy and safety, therefore it is the only HZ vaccine recommended by NIAC.

23.7.1 Shingrix

Shingrix is a non-live, recombinant vaccine containing varicella zoster virus glycoprotein E antigen adjuvanted with $AS01_B$.

Licensed indications

Prevention of herpes zoster and post herpetic neuralgia (PHN) in:

- those aged 50 years and older
- those aged 18 years and older at increased risk of herpes zoster.

Storage

The vaccine should be stored at +2°C to +8°C and protected from light. After reconstitution the vaccine should be used promptly; if this is not possible, store at +2°C to +8°C and discard if not used within six hours.

Dose, route of administration and schedule

The dose is 0.5 ml IM or SC in the deltoid region. Two doses are required 2-6 months apart. For those who are or might become immunodeficient or immunosuppressed due to disease or therapy, and who would benefit from a shorter vaccination schedule, the second dose can be given one to two months after the initial dose.

The need for a booster has not been established.

Efficacy

Immunocompetent

Two clinical trials in immunocompetent recipients who received two doses, with a median follow up time of 3.2 years, showed efficacy against HZ of 96.6%% in those aged 50-59 years, 97.4% in those aged 60-69 years, 90.0% in those aged 70-79 years and 89.1% in those aged 80 years and older. Postherpetic neuralgia (PHN) did not develop in any vaccine recipient less than 70 years of age. The efficacy against PHN in those aged 50 years and older was 88.8%.

Shingrix protects against HZ for at least ten years in immunocompetent recipients.

Immunocompromised

In autologous HSCT recipients aged 18 years and older who received two doses of RZV, vaccine efficacy against HZ overall was estimated at 68.2% with a median follow up time of 21 months. A separate post-hoc subgroup analysis of the trial data by age reported a vaccine efficacy against HZ in those aged 18-49 years of 72%. Post hoc efficacy analysis of patients aged 18-49 years with haematological malignancies reported a vaccine efficacy against HZ of 87.2% at 13 months.

The duration of immunity in HSCT recipients and in those with haematological malignancies, solid organ tumours, renal transplant and HIV is not known beyond 12 to 24 months.

Effectiveness

Immunocompetent

Shingrix has been shown to be 85.5% effective in immunocompetent adults aged 50 years and older with a median follow up time of seven months. Effectiveness ranged from 85.6% in those aged 50-59 years to 80.3% in those aged 80 years and older.

Immunocompromised

One and two dose real world vaccine effectiveness (VE) of Shingrix was estimated at 56.9% and 70.1% respectively in a US study of adults aged 65 years and over, including those with autoimmune conditions or immunocompromising conditions. The median follow up times for the group who received one dose and the group who received two doses were 2.9 months and 7.1 months respectively. Two dose VE was not significantly lower

for adults aged 80 years and older for second doses received at ≥180 days, or for individuals with autoimmune conditions. Two dose VE against PHN was estimated at 76.0%.

23.8 Herpes zoster vaccine recommendation

23.8.1 Adults aged 65 years and older

Immunisation with recombinant zoster vaccine (RZV; Shingrix) of all those aged 65 years and older is recommended, due to the greater burden and severity of disease and postherpetic neuralgia (PHN) in this age group.

23.8.2 Vaccination of other adults in risk groups

Immunisation with RZV (Shingrix) is recommended for the following:

1. All adults aged 50 years and older with the following immunocompromising conditions: solid organ transplant recipients, cancer, primary or acquired cellular and combined immune deficiencies and immune mediated inflammatory disorders
2. All HSCT recipients aged 18 years and older

Immunisation with RZV (Shingrix) should be considered for patients aged 18-49 years and older with immunocompromising conditions in particular solid organ transplant recipients, those with haematological malignancies and those with advanced or untreated HIV (CD4 count <200 cells/µl), in consultation with a treating specialist physician.

As the vaccine is not part of the national immunisation programme, those who wish to receive it should consult with their GP or pharmacist.

The vaccine may be given to those who have had zoster. It is prudent to defer vaccination for 12 months after the zoster has resolved so that the vaccine can produce a more effective immune response.

The immune response to Shingrix is unaffected by prior vaccination with Zostavax.

Contraindications

Anaphylaxis to any of the vaccine *constituents.*

Precautions

Acute severe febrile illness - defer until recovery.

Shingrix should be given with caution to those with thrombocytopenia or any coagulation disorder since bleeding may occur following IM administration to these subjects. The SC route may be used.

It is preferable to defer Shingrix during pregnancy.

Coadministration
Shingrix can be given concomitantly with unadjuvanted inactivated seasonal influenza vaccine, PPV23, PCV13, Tdap, or COVID-19 mRNA vaccine. The vaccines should be administered at different injection sites.

Adverse reactions
Common adverse events are listed below, a full list of adverse reactions may be found in the SmPC.

Local: Very common: erythema, pain, swelling.
Common: pruritus.

General: Very common: abdominal pain, diarrhoea, fatigue, fever, headache, myalgia, nausea, vomiting.
Common: malaise.

23.9 Post exposure prophylaxis

The aim of post exposure prophylaxis is to protect individuals at high risk of developing severe varicella disease and also those who may transmit infection to those at high risk (such as health care workers or household contacts).

Whether active (varicella vaccine), passive immunisation (varicella zoster immunoglobulin VZIG) or antiviral medication is offered to a susceptible person with a history of varicella or zoster exposure depend on the host, the type of exposure and the time since exposure.

23.9.1 Protection of contacts with vaccine

Immunisation of susceptible contacts with varicella vaccine may prevent infection or modify disease course. Non-immune people from 12 months of age who have had a significant exposure to varicella or herpes zoster should be given varicella vaccine. The vaccine should be given within five days after exposure, and preferably within three days (see Table 23.1).

23.9.2 VZIG prophylaxis for contacts

Prophylaxis is recommended for individuals who fulfil all the following criteria:

- Had significant exposure to varicella or zoster. The risk of acquiring infection from an immunocompetent individual with non-exposed zoster lesion, e.g., thoracolumbar, is remote.

  and

  Have an increased risk of severe varicella (e.g., immunocompromised, pregnant, neonates in the first week of life born to non-immune women, infants in neonatal units)

  and
- Are non-immune (no VZV antibodies)

Significant exposure is defined based on:

- type of VZV infection in the index case (Table 23.1)
- timing of exposure in relation to the onset of rash in the index case
- proximity and duration of contact.

Table 23.1. Criteria for defining significant exposure to VZV

Type of VZV infection in index case	Timing of exposure in relation to onset of rash in index case	Proximity and duration of contact (any of the following)
Varicella or disseminated zoster	From 48 hours before onset of rash until crusting of lesions	Contact in same room (e.g. in a house, classroom or a 2-4 bed hospital bay) for an hour or more. Face to face contact, within one metre e.g., while havinga conversation (usually less than five minutes). Susceptible high risk contacts in large open wards, particularly in paediatric wards where degree of contact may be difficult to define.
Localised zoster in an immunocompromised patient (as viral shedding may be greater)	Day of onset of rash until crusting of lesions.	

23.9.3 Recommendations for post exposure prophylaxis

23.9.3.1 Neonates and infants (Figure 23.3)

VZIG is recommended for:

- Neonates who are exposed to varicella in the mother from seven days before to seven days after delivery. Approximately half of these infants may develop varicella despite immunoprophylaxis, but the disease is usually modified. IV aciclovir treatment may occasionally be required.

These neonates must receive VZIG as early as possible in the incubation period, because neonatal mortality without VZIG is up to 30%.

- VZ antibody-negative infants
  - exposed to varicella or zoster (other than in the mother) in the first seven days of life.
  - of any age, exposed to varicella or zoster while requiring intensive or prolonged special care.

The following infants may not have maternal antibodies despite a positive maternal history of varicella and should be tested to determine their VZ antibody status in the event of a contact:

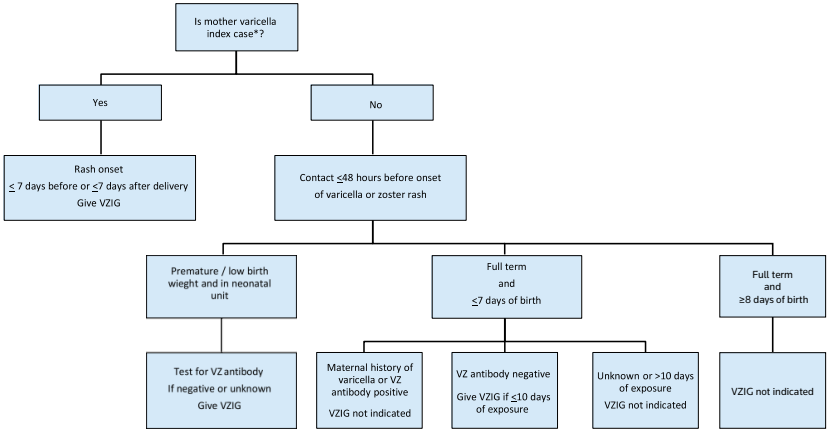
- born at less than 28 weeks' gestation
- weigh less than 1,000g at birth
- infants 60 days of age or more still requiring intensive or prolonged special care
- had repeated packed red cell infusions.

Other infants whose mothers have a positive history of varicella and/or VZV antibodies will usually have maternal antibodies and do not require VZIG.

VZIG is **not** indicated for full term infants exposed to VZV (either varicella or zoster) more than seven days after delivery or if exposure was more than 48 hours before onset of varicella or zoster rash in the index case.

People receiving monthly high-dose IV HNIG are likely to be protected and may not need VZIG if they received the last dose of HNIG within three weeks before exposure.

Figure 23.3 Use of VZIG in neonates exposed to VZV



23.9.3.2 Pregnancy (Figure 23.4)

Non-immune women significantly exposed to varicella* at any stage of pregnancy should be offered post exposure prophylaxis (PEP). This can take the form of either antivirals (oral aciclovir) or VZIG.

The decision on which prophylaxis to give should be made in line with local hospital guidelines and following discussion with the mother regarding the risks and benefits of each option.

Management of varicella infection in pregnancy should be discussed urgently with an obstetrician/microbiologist/ID consultant and consideration given to the use of an antiviral drug.

There is sufficient evidence to state that immunoprophylaxis with oral aciclovir is as effective as VZIG. In general, aciclovir should be considered the first-line option for prophylaxis and VZIG should only be offered if the woman is unable to take oral antivirals, for example, due to malabsorption or renal toxicity. The preference for aciclovir is because of ease of administration, limited VZIG supply and the theoretical potential for donor-related illness from VZIG.

There is little evidence that immunoprophylaxis will prevent congenital varicella syndrome following significant exposure of a non-immune mother in the first 20 weeks of pregnancy.

The date of exposure is defined as: the date of contact in a single exposure event, the date of first contact if exposure is on multiple occasions, or the date of rash onset in the index case if they are a household contact.

*Non-immune pregnant women with significant exposure to varicella vaccine related rash should contact their treating physician as they may be eligible for post exposure prophylaxis.

Antiviral post exposure prophylaxis
Oral aciclovir 800 mg four times daily (i.e., six hourly) from day 7-14 post exposure is the recommended antiviral.

Oral valaciclovir 1,000 mg three times daily may be used as an alternative, but the increased cost and comparative paucity of trial data should be taken into consideration.

If the woman presents later than day seven post exposure, a seven day course of antivirals can be started up to day 14 after exposure. Given the relatively short half-life of aciclovir, if a subsequent exposure occurs, an additional course of seven days of antivirals may be administered following repeat VZV IgG testing and a risk assessment.

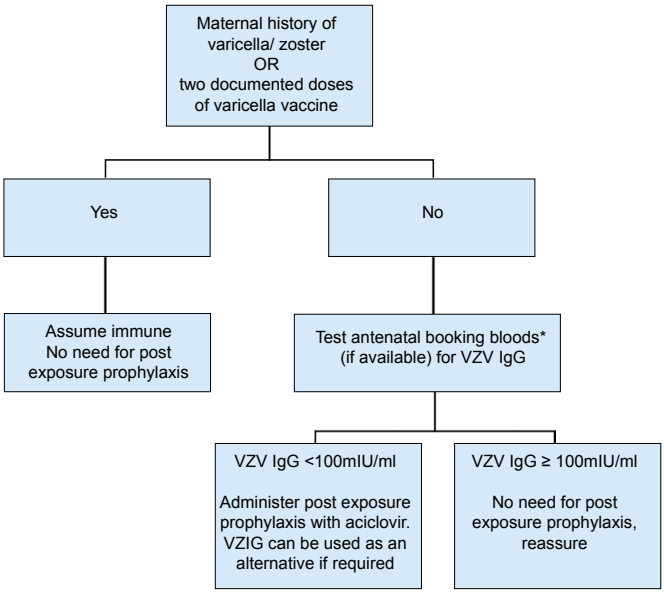
Though aciclovir is not licensed in pregnancy, there is robust safety data to recommend its use in the setting of VZV disease and exposure. A detailed review of the safety data is presented in the HSE Medication Guidelines for Obstetrics and Gynaecology First Edition, Volume 2, Antimicrobial Safety in Pregnancy and Lactation (2017)

VZIG post exposure prophylaxis

VZIG should be administered as soon as possible and ideally within 96 hours of contact. It can be administered up to 10 days post exposure.

If a subsequent exposure to varicella occurs three weeks or more after the first dose of VZIG, an additional dose may be administered following repeat VZV IgG testing and a risk assessment.

Figure 23.4 Post exposure prophylaxis for pregnant women exposed to VZV



*A repeat serum sample should be taken for VZV in cases of repeated exposure to varicella in the same pregnancy if the booking bloods or most recent serology demonstrate non immunity

23.9.3.3 Immunocompromised contacts (Figure 23.5)

Immunocompromised contacts who are VZV non-immune and who have significant exposure to varicella* or zoster may require VZIG. This includes adults and children with no history of varicella and/or a negative immune status, receiving immunosuppressive therapy including steroids, cytostatic agents, radiotherapy, recent stem cell transplantation, or who have congenital or acquired immunodeficiency disorders and are not receiving replacement therapy with immunoglobulin (Chapter 3).

Immunocompromised contacts should be tested for VZV antibody *regardless of history of varicella*. If seronegative, VZIG is indicated. Testing will rarely be required outside normal working hours. VZIG administration should ideally not be delayed more than seven days after initial contact. If an immunosuppressed contact is antibody positive, VZIG is not indicated.

*Non-immune immunocompromised persons with significant exposure to varicella vaccine related rash should contact their treating physician as they may be eligible for post exposure prophylaxis.

Those with immunoglobulin deficiencies who are receiving replacement therapy with immunoglobulin do not require VZIG.

VZV IgG seronegative (non-immune) HIV positive contacts with CD4 cell count <15% should be considered for both VZIG and antiviral prophylaxis with aciclovir (800 mg four times daily) or valaciclovir (1 g three times daily) starting from day seven after exposure and continuing for seven days.

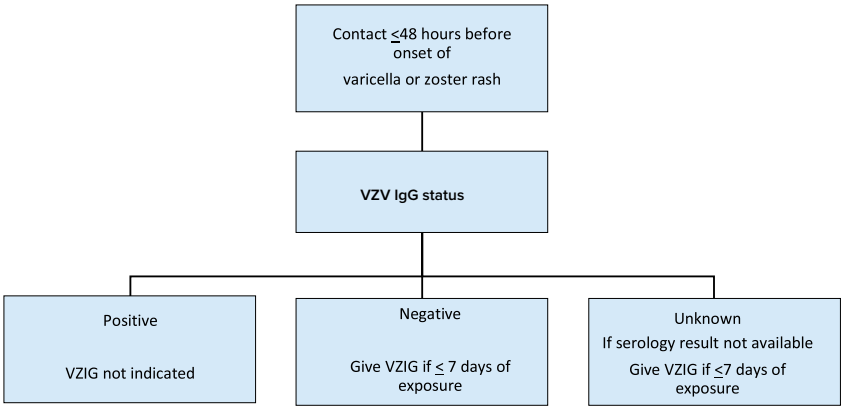
Varicella vaccine should be considered for VZV IgG seronegative HIV-positive contacts with CD4 cell count ≥15% between three and five days after exposure. A second dose should be given three months later.

Those born and raised overseas are less likely to be immune so may require serological testing to check immunity.

Immunocompetent contacts with a definite history of varicella are immune so neither serology nor immunoprophylaxis are necessary. The majority of adults and a substantial proportion of children without a definite history of varicella are VZV IgG positive. Those without a definite history, who are being considered for VZIG, should be tested for VZV IgG.

VZV IgG detected in patients who have received blood or blood products in the previous three months may have been passively acquired. Retesting in the event of subsequent exposure is required, as the patient may have become VZV IgG negative.

Figure 23.5 Guidance for use of VZIG in immunocompromised persons exposed to VZV



23.9.3.4 Management of HCW exposure to varicella or zoster

Non-immune HCWs who have had significant exposure to VZV (see Table 23.1) should be excluded from contact with high-risk patients from 8-21 days after exposure.

Post exposure prophylaxis is not indicated for non-immune HCWs exposed to varicella or zoster unless they are immunocompromised or pregnant.

HCWs with localised zoster on a part of the body that can be covered with a bandage and/or clothing may be allowed to continue working, except with high-risk patients; in that case an individual risk assessment should be carried out.

23.10 VZIG preparations, dose and administration

VZIG should be given as soon as possible after exposure, ideally within 72 hours; It may be given up to 10 days.

23.10.1 Human Varicella-Zoster Immunoglobulin 100 IU/ml solution for injection.

Each vial contains 250 mg human varicella-zoster immunoglobulin (VZIG).

Licensed indications

Prophylaxis against varicella zoster virus (VZV) infection in the following at risk patients exposed to varicella (chickenpox) or herpes zoster:

- pregnant women with negative VZV IgG status especially up to early in the third trimester (see Section 23.9.3.2)
- neonates whose mothers develop varicella infection within seven days before and seven days after delivery
- neonates whose mothers have no history of varicella infection or vaccination and/or VZV IgG negative
- premature infants less than 28 weeks' gestation or newborns with low birth weight
- children and adults with no history of varicella infection or vaccination and/or VZV IgG negative, with immunocompromise due to disease or treatment and are not receiving replacement therapy with immunoglobulin.

Dose, route of administration and schedule

0 - 5 years	250 mg (1 vial) IM
6 - 10 years	500 mg (2 vials) IM
11 - 14 years	750 mg (3 vials) IM
15 years and older	1,000 mg (4 vials) IM

If a second exposure to chickenpox occurs three weeks or more after the first dose of VZIG, a second dose is required.

Method of administration

VZIG should be given IM in the deltoid or anterolateral thigh. If a large volume, over 1-2 ml for infants or children, or over 3-5 ml for adults is required, it should be given in divided doses at different sites.

If IM administration is contraindicated (severe bleeding disorders), the injection can be administered SC. However, there are no clinical efficacy data to support SC administration.

Contraindications

Anaphylaxis to IgG, IgA or any of the vial contents.

Precautions

Immunoglobulin administration may interfere with the immune response to MMR and Varicella vaccines, see Chapter 2 Table 2.6 for deferral times.

Adverse reactions

Local:	Common: swelling, soreness, redness.
General:	Chills, headache, dizziness, malaise, fever, nausea, vomiting, allergic reactions, arthralgia, hypotension, moderate low back pain and anaphylaxis may occur occasionally. Their frequency is not known.

For special warnings and precautions, and a full list of undesirable effects see the SmPC.

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