



UK Health
Security
Agency

Guidelines on post exposure prophylaxis (PEP) for varicella/shingles (April 2022)



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Document history

Date	Reason for change	Issue number
April 2022	<p>New document created from merging of the 'PHE Guidance for issuing varicella-zoster immunoglobulin (VZIG) and 'PHE Updated guidelines on post exposure prophylaxis (PEP) for varicella/shingles. Updated information on transmission and incubation period, removal of Groups A and B classification of immunosuppressed individuals for purposes of PEP and advice that the recommended post exposure prophylaxis for susceptible individuals is antivirals except for neonates exposed within one week of delivery (either in utero or post-delivery for whom VZIG continues to be recommended).</p> <p>Reformatted in UKHSA style and branding</p>	1.0

A. Introduction

Chickenpox (varicella) infection in immunosuppressed individuals, pregnant women and neonates can result in severe and even life-threatening varicella disease. Post-exposure prophylaxis (PEP) is recommended to attenuate disease and reduce the risk of complications such as pneumonitis, rather than to prevent infection in these at-risk individuals.

Historically this has primarily been achieved through the timely administration of varicella zoster immunoglobulin (VZIG) in those at risk, but in response to a severe national shortage of VZIG due to manufacturing issues from the sole UK supplier in July 2018, an expert working group was convened by the Immunisation Division at Public Health England (PHE) (now UK Health Security Agency, UKHSA) to review the evidence on the safety and efficacy of antiviral agents as an alternative for post-exposure prophylaxis (PEP). Restrictions on the use of VZIG were implemented to prioritise stock for the most vulnerable groups, for whom antivirals were not considered appropriate, whilst supplies of VZIG were limited. Antivirals were advised as suitable alternatives in immunosuppressed contacts and pregnant women exposed from 20 weeks gestation. A series of evaluations commenced to gather further evidence on the efficacy of antivirals as PEP in pregnant women and immunosuppressed groups as well as an acceptability survey of health professionals and patients on antiviral use.

The expert working group reconvened in April 2019 to review the VZIG supply situation and available data from the ongoing evaluations. The group considered a number of factors relating to current and future immunoglobulin supply in informing their advice.

These included:

- the fact that VZIG was procured by PHE from a sole supplier and the limited availability of a suitable alternative immunoglobulin product – interruptions in supply had occurred in the past and this remained a potential risk in the future
- global supplies of a range of immunoglobulin products had been limited in recent years and supplies were likely to remain constrained in the future – therefore, the ability to identify suitable alternative products not derived from blood is important

In light of the resumption of VZIG supplies and available evidence on safety and efficacy of antivirals as PEP, updated interim guidance was published by PHE in June 2019. This has now been reviewed in light of further data, and consolidated into a single document with the recommended post-exposure prophylaxis for different risk groups.

In summary, antivirals are now recommended for post-exposure prophylaxis for all at risk groups apart from susceptible neonates exposed within one week of delivery (either in utero or post-delivery). VZIG is recommended for those for whom oral antivirals are contraindicated.

B. Post-exposure risk assessment: does the person need PEP?

Post exposure prophylaxis is recommended for individuals who fulfil all of the following 3 criteria:

- significant exposure to chickenpox (varicella) or shingles (zoster) during the infectious period
- at increased risk of severe chickenpox such as immunosuppressed individuals, neonates and pregnant women
- no antibodies to varicella-zoster virus (VZV) – urgent VZV antibody testing can be performed within 24 hours

1. Infectious period and routes of transmission

Chickenpox infection is transmitted from person to person primarily by inhalation of aerosols from or direct contact with vesicular fluid from varicella or herpes zoster lesions, although transmission may occur if infected respiratory tract secretions are aerosolised. Although historically, the infectious period for chickenpox was generally considered as being from 48 hours before, to 4 to 7 days after, onset of rash, a recent review suggested that transmission rarely occurs before the onset of rash, (1) and may continue until all the lesions have crusted over.

In immunocompetent individuals, as a general rule the infectious period the time should be taken as being from 24 hours prior to rash onset to 5 days after rash. For immunosuppressed individuals, it is harder to generalise and therefore the infectious period should be taken from 24 hours prior to rash onset until all lesions have crusted over.

Shingles infection is primarily transmitted by direct contact with vesicle fluid in immunocompetent individuals but may be transmitted via infected respiratory secretions from immunosuppressed patients. The infectious period for localised and disseminated shingles is considered as the time from onset of rash until all of the lesions have crusted over.

2. Definition of a significant exposure to varicella-zoster virus (VZV)

Three aspects of exposure to VZV during the infectious period are relevant when considering the need for post-exposure prophylaxis (PEP) for a susceptible high risk individual:

Type of VZV infection in index case:

PEP should be issued only for those in contact with chickenpox or those in contact with:

- disseminated shingles
- immunocompetent individuals with exposed shingles lesions (for example ophthalmic shingles)
- immunosuppressed individuals with localised shingles on any part of the body in whom viral shedding may be greater

The risk of acquiring infection from contact with an immunocompetent individual with non-exposed shingles lesions (for example thoraco-lumbar) is remote and therefore is not an indication for PEP.

Timing of the exposure

PEP should be offered to contacts in a specified risk group (see section D for definitions):

- where there is continuous exposure to a case of chickenpox/ shingles (see definitions in 'Type of VZV infection in index case' above), for example household member, nursery or care worker
- where there has been more than one exposure to a case of chickenpox/ shingles (for example family friend who visited on more than one occasion during the infectious period)
- where there has been a single exposure to a case of chickenpox during the infectious period from 24 hours before onset of rash until 5 days after rash appearance in immunocompetent individuals and until all lesions have crusted over for immunosuppressed individuals
- where there has been a single exposure to a case of shingles (see definitions in 'Type of VZV infection in index case' above) during the infectious period from onset of rash until the lesions have crusted over (in immunocompetent individuals, this is usually 5 days after rash appearance)

Closeness and duration of contact

In addition to household contacts, the following contacts in the specified risk groups require PEP:

- those in the same small room (for example in a house or classroom or a 2 to 4 bed hospital bay) for a significant period of time (15 minutes or more)
- face to face contact, for example while having a conversation

- immunosuppressed contacts on large open wards, where air-borne transmission at a distance has occasionally been reported, particularly in paediatric wards where the degree of contact may be difficult to define

3. Assessment of susceptibility

The administration of varicella zoster immunoglobulin (VZIG) is unlikely to confer any additional benefit for patients who already have varicella antibody (VZV IgG) and therefore VZIG is not recommended for individuals with adequate levels of VZV IgG. Assessment of susceptibility will depend on the history of previous infection or vaccination, and the underlying clinical condition.

For immunocompetent individuals including pregnant women, a history of previous chickenpox, shingles or 2 doses of varicella vaccine is sufficient evidence of immunity. In those without such a history, urgent antibody testing should be undertaken on a recent blood sample (booking blood samples are acceptable for pregnant women if available). PEP (antivirals or VZIG, if antivirals contraindicated) should be offered if VZV IgG is <100 mIU/ml.

For immunosuppressed patients, a history of previous infection or vaccination is not a reliable history of immunity and VZV antibody levels should be checked urgently. Individuals with VZV antibody levels of 150 mIU/ml or greater are unlikely to benefit from VZIG, and therefore individuals with VZV IgG <150 mIU/ml in a quantitative assay, or negative or equivocal in a qualitative assay should be offered PEP. Qualitative or quantitative antibody testing is required for all immunosuppressed patients where VZIG is being considered (such as individuals in whom antivirals are contraindicated).

C. Types of post-exposure prophylaxis

1. Antivirals (aciclovir or valaciclovir)

Oral aciclovir (or valaciclovir) is now the first choice of PEP for susceptible immunosuppressed individuals, all susceptible pregnant women at any stage of pregnancy and infants at high risk (see sections D.1, D.2 and D.3). Individuals in these groups who are exposed to chickenpox/shingles should be assessed and for those identified as susceptible antivirals (oral aciclovir or valaciclovir) should be given from day 7 to day 14 after exposure. The day of exposure is defined as the date of onset of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s) respectively.

If the patient presents after day 7 of exposure, a 7 day course of antivirals can be started up to day 14 after exposure, if necessary.

The dose of aciclovir is based on the adult and Children's British National Formularies (BNFs). (2, 3). There is limited evidence for dosing for valaciclovir prophylaxis but given the improved

bioavailability, fewer daily doses and better side effect profile, valaciclovir may be preferred. The dosage of valaciclovir is based on the therapeutic dose for chickenpox.

Reason for starting antivirals at day 7 after exposure

In a study evaluating the comparative effectiveness of a 7 day course of aciclovir given either immediately after exposure or starting at day 7 after exposure to healthy children, the incidence and severity of varicella infection was significantly higher in those given aciclovir immediately after exposure (10 of 13 (77%) who received aciclovir immediately developed clinical varicella compared with 3 of 14 (21%) who started aciclovir at day 7) (4).

A 7 day post exposure prophylaxis course of aciclovir or valaciclovir is therefore recommended to start from day 7 after exposure.

Potential side effects of aciclovir and valaciclovir

The most commonly reported side effects from aciclovir include dizziness, headache, nausea, vomiting, diarrhoea, abdominal pain, skin rashes, photosensitivity, pruritus, urticaria and fatigue. Further information about side effects on aciclovir and valaciclovir are available in the BNFs. (2,3).

Contraindications and precautions to aciclovir and valaciclovir

In individuals with renal impairment or intestinal malabsorption, for example inflammatory bowel disease, VZIG may be considered. The dose of aciclovir may need to be adjusted in patients with renal impairment. Individuals with glomerular filtration rates less than 10 mL/minute/1.73m² may need the frequency or dose altered (please see BNF).

If VZIG is considered, it is important to demonstrate that the patient will benefit from the blood product by demonstrating that they are sero-negative with VZV IgG antibody levels < 150 mIU/ml for immunosuppressed patients and < 100 mIU/ml for pregnant women. For immunosuppressed patients only, if time does not permit quantitative testing, a qualitative test must be performed and shown to be negative or equivocal. Similarly for pregnant women who are unable to take antivirals due to renal impairment, intestinal malabsorption or hyperemesis, if time does not permit quantitative testing, a qualitative test must be performed and shown to be negative.

Table 1. Recommended doses of oral antivirals

	Oral Aciclovir	Oral Valaciclovir
Infants over 4 weeks to children under 2 years age	10mg/kg 4 times daily, days 7 to 14 after exposure	Not recommended
Children 2 to 17 years of age	10mg/kg (up to a maximum of 800mg), 4 times daily, from days 7 to 14 after exposure	20 mg/kg (up to a maximum 1,000mg) 3 times daily, from days 7 to 14 after exposure
Adults	800mg 4 times daily, from days 7 to 14 after exposure	1,000mg 3 times daily, from days 7 to 14 after exposure

Individuals on long term aciclovir or valaciclovir prophylaxis, for example post-haematopoietic stem cell transplant, may require their dose of aciclovir to be temporarily increased to the dosage as given in Table 1 above.

Off label use of aciclovir and valaciclovir

Although aciclovir and valaciclovir are not currently licensed for post-exposure prophylaxis for chickenpox, their use in the treatment of chickenpox is well established. Clinicians are able to prescribe medicines outside the terms of the licence when it is in the best interest of the patient on the basis of available evidence. This evidence has been considered and recommended by the PHE/UKHSA convened expert working group (see Appendix 1 for membership).

[Further advice on off-label prescribing is on the MHRA website.](#)

When current practice supports the use of a medicine outside the terms of its licence, the MHRA advise that it may not be necessary to draw attention to this when seeking consent from patients. However, it is good practice to give as much information as patients or carers require or which they may see as relevant.

Further doses of PEP following second exposure

If there is a second or subsequent exposure to chickenpox further courses of antivirals can be initiated starting 7 days after the date of onset or exposure.

2. Human varicella-zoster immunoglobulin (VZIG)

For individuals who are unable to take oral antivirals, and for susceptible neonates exposed within one week of delivery (in utero or post-delivery), varicella-zoster immunoglobulin should be given. Varicella-zoster immunoglobulin (VZIG) is prepared by Bio Products Limited (BPL) from the pooled plasma from non-UK blood donors and is dispensed in vials of 250 mg (minimum 100 IU/ml). VZIG is issued by the Rabies and Immunoglobulin Service, UK Health

Security Agency, Colindale (tel: 0330 128 1020), and some local UK HSA laboratories, following a risk assessment of the exposed individual.

Dosage and timing of VZIG for prophylaxis

Table 2: VZIG dosage

0 to 5 years	250mg	By slow intramuscular injection
6 to 10 years	500mg	
11 to 14 years	750mg	
15 years and older	1,000mg	

When a large-volume injection such as VZIG is to be given, it should be administered deep into a large muscle mass. If more than 3ml is to be given to young children and infants, or more than 5ml to older children and adults, the immunoglobulin should be divided into smaller amounts and given into different sites. The upper outer quadrant of the buttock can be used to administer VZIG injection in neonates and infants.

VZIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts) of the day of exposure. The day of exposure is defined as the date of the onset of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s). If a second contact is reported beyond 10 days (7 days for immunosuppressed) of the first exposure, then repeat assessment based on the date of the second exposure should be made to determine the need for, and benefit from, additional PEP. See 'Subsequent exposure to chickenpox/ shingles' in relevant risk group section below.

Individuals receiving regular IVIG replacement therapy do not require VZIG if the most recent dose was administered \leq 3 weeks before exposure.

Further doses of VZIG following second exposure

Individuals who have previously received VZIG or IVIG as VZV post-exposure prophylaxis require a new risk assessment if a second exposure occurs. If the second exposure occurs:

- within 3 weeks of administration of VZIG or IVIG, further PEP is not required
- between 3 and 6 weeks following administration of VZIG or IVIG, further PEP (dose of VZIG) should be administered without further testing
- more than 6 weeks following administration of VZIG or IVIG, retesting of a new sample is required

3. Intravenous immunoglobulin (IVIG)

Contacts with bleeding disorders who cannot receive antivirals or be given an intramuscular injection should be given intravenous human normal immunoglobulin (IVIG) at a dose of 0.2g per kg body weight (4ml/kg for a 5% solution) instead. This will produce serum VZV antibody levels equivalent to those achieved with VZIG.

IVIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts), of the first contact, but can be given later if necessary.

Supplies of intravenous immunoglobulin (IVIG), if indicated, should be available from the local hospital pharmacy or from the manufacturers. IVIG is not issued by UKHSA.

D. Guidance for specific risk groups

1. Immunosuppressed individuals

All immunosuppressed individuals as defined in chapter 6 (Immunisation against infectious disease – the Green Book (5); Annexe 1) are at risk of severe chickenpox and should be assessed for the need for prophylaxis following a significant exposure.

Efficacy and safety of VZIG and aciclovir in immunosuppressed individuals

Efficacy of VZIG in preventing severe complications of chickenpox in immunosuppressed individuals was demonstrated in a follow up of 122 children in high risk groups who received VZIG following an exposure, including 80 seronegative children (6). Of the 27 exposed in the household, 18 seroconverted (14 with symptoms). Seroconversion in hospital exposures was considerably lower (6 of 43 with 3 developing symptoms). Of the 17 symptomatic cases, only 2 were severe but in both of these VZIG was administered outside of the optimal window.

Efficacy of aciclovir for post exposure prophylaxis in immunocompromised individuals has been evaluated in a small number of retrospective studies. The findings from these have varied from reporting no breakthrough varicella infections following aciclovir while others report a rate of 3–22% (7) In a retrospective observational study evaluating the effectiveness of aciclovir post exposure prophylaxis in 141 contacts exposed to varicella in a paediatric setting between 2000 and 2007 in a Japanese hospital, the rate of secondary infection was 2.1% in all contacts and 3.1% for immunocompromised contacts (8). This compares with a secondary infection rate of 18% in those not receiving any post exposure prophylaxis (RR 8.5 (95%CI: 1.6-45.9)).

In a recent UK observational study (PEPtalk3) of 105 immunosuppressed children with underlying haematology or oncology diagnoses exposed to VZV and requiring PEP, 87 where

treated with antivirals (aciclovir or valaciclovir) compared to 18 children who received VZIG. Five children (of 84) who received aciclovir developed break through infections (6.0%) (3 mild and 2 moderate severity) compared with 2 children (11.1%) who received VZIG (one mild and one moderate severity). Although the results were not significantly different (risk difference: -5.2% (95% CI -20.5% to 10.2%), $p=0.60$), treatment with antivirals was no worse than VZIG prophylaxis (9).

With respect to safety, aciclovir has a good safety profile for immunosuppressed individuals and this compares with the potential (albeit low) risk from VZIG, as a blood product.

The 2002 Royal College of Paediatrics and Child Health (RCPCH) guidelines for the 'Immunisation of the Immunocompromised Child' recommended that aciclovir or VZIG can be offered to these individuals (10). As such, it has been routine practice in approximately 50% of paediatric oncology centres across the UK to preferentially use antivirals for PEP in their paediatric population up until 2019 when the national recommendation to preferentially use antivirals was made.

Immunosuppressed individuals presenting with chickenpox

If, despite having received VZIG, IVIG or taken prophylactic aciclovir or valaciclovir, an immunosuppressed individual presents with a chickenpox rash, they should be changed onto a therapeutic dose of antivirals, starting from the day of onset of the rash. If severe chickenpox develops, they will need an urgent assessment and may require to be hospitalised and given intravenous (IV) aciclovir.

Subsequent exposure to chickenpox or shingles

Immunosuppressed individuals who have a second or further exposures, should be risk assessed as above. Given the rates of seroconversion with both VZIG and aciclovir, ideally patients should have a repeat VZV antibody test prior to considering a course of aciclovir or valaciclovir. Given the short half life of aciclovir or valaciclovir, if there is a second exposure immediately after a course of antivirals, a second risk assessment and course should be given in the same way starting 7 days after the subsequent exposure.

Inadvertent administration of chickenpox or shingles vaccine to immunosuppressed individuals

Immunosuppressed individuals who are inadvertently vaccinated with the live attenuated chickenpox/ shingles vaccines should be urgently assessed by a clinician to establish the degree of immunosuppression and treated with antivirals from day 7 as above if susceptible.

2. Pregnant contacts

Why PEP is recommended for pregnant women

Chickenpox infection during the first 20 weeks of pregnancy can lead to fetal varicella syndrome, which includes microcephaly, cataracts, growth retardation limb hypoplasia, and skin scarring. Chickenpox can cause severe maternal disease and this risk is greatest in the second or early in the third trimester.

The rationale for PEP in pregnant women is two-fold: reduction in severity of maternal disease and theoretical reduction in the risk of fetal infection for women contracting varicella in the first 20 weeks of pregnancy. In late pregnancy, PEP may also reduce the risk of neonatal infection. However, given the risks of severe neonatal varicella in the first week of life, VZIG is also given to infants born within 7 days of onset of maternal varicella.

In the absence of PEP, the risk of developing varicella in susceptible contacts is high with 13 of 18 (72%) of seronegative pregnant women developing varicella following a significant exposure (11).

Further information about chickenpox in pregnancy is provided by the [Royal College of Obstetrics and Gynaecology at Royal College of Obstetrics and Gynaecology Chickenpox in Pregnancy \(Green-top Guideline No.13\)](#)

Safety of PEP in pregnancy

VZIG is a concentrated preparation of antibodies against chickenpox (varicella) derived from healthy non-UK blood donors. As with any other blood product, although screened for HIV, Hepatitis B and C, there remains a very low risk of transfusion transmitted infections.

Although oral aciclovir and valaciclovir (prodrug of aciclovir) are not licensed in pregnancy, there is extensive evidence of safety in pregnancy, including from 2 large registries of infants whose mothers were exposed to aciclovir in pregnancy. Aciclovir is also recommended for treatment of chickenpox in pregnant women who are 20 weeks or more gestation. From follow up across 24 countries between 1984 to 1999 of over 1,200 pregnancies that received either oral or IV aciclovir across all stages of pregnancy, no unusual defects or patterns of defects were observed (12). In a Danish national cohort study of 1,804 exposures to antiviral agents (aciclovir, valaciclovir, famciclovir) in pregnancy, no increase in major birth defects was reported in women exposed to either aciclovir or valaciclovir in the first trimester (13).

Efficacy of PEP in pregnant women

The efficacy of VZIG in preventing clinical chickenpox is known to be suboptimal and the results from studies are consistent. In a study of 212 seronegative women who were given VZIG within 10 days of exposure 41% developed clinical varicella infection (14). VZIG given within the first 3 days following exposure had the same efficacy (63 of 153 developed varicella). In an unpublished study from Kings College Hospital of 23 seronegative women who received VZIG

<20 weeks, 8 developed clinical chickenpox; of the 7 women more than 20 weeks, who received VZIG, 5 developed clinical chickenpox (overall 43%). Similarly, in a study of 20 years' experience in Italy, of 50 pregnant seronegative women followed up after receipt of VZIG as PEP, 21 of 50 (42%) developed clinical chickenpox (11).

In a Birmingham (UK) study, outcome information was obtained on 21 exposed women with IgG levels of <150mIU/ml who received VZIG. Of these 5 (24%) developed clinical chickenpox, similar to the proportion of women developing chickenpox in the absence of treatment (6 of 23; 26%) (15).

In a recent PHE/UKHSA study of confirmed seronegative pregnant women exposed to chickenpox, 53 (36.6%) of 145 individuals treated with VZIG went on to develop chickenpox, compared to 8 (30.8%) of 26 individuals treated with aciclovir. Although the difference is not statistically significant, aciclovir was as good as VZIG at preventing chickenpox infection. In addition 14 of 145 (10%) of the women receiving VZIG complained of pain at the site of injection, compared to no reported side-effects in the aciclovir group (16). These results are similar to those collected from a sentinel network of virologists in 2019 to 2020 where none of 12 exposed women who received aciclovir developed chickenpox compared to one of 9 who received VZIG. Anecdotally it was preferred by the women and negated a hospital or GP attendance to receive the treatment. In many cases aciclovir is used based on the clinical history alone and without confirming that the patient is VZV IgG seronegative.

There is little if any available data on the efficacy of aciclovir in preventing congenital varicella infection and prevention of transplacental infection of the foetus following potential exposures in the first 19 weeks of pregnancy.

Risk assessment for pregnant women

Pregnant contacts with a positive history of chickenpox/ shingles or 2 recorded doses of varicella vaccine do not require testing or PEP (see table 3). Antibody responses following vaccination may not be detectable and therefore results of VZV IgG testing in patients known to be vaccinated cannot be used to determine susceptibility. The history of vaccination should be used instead to determine need for post-exposure prophylaxis. Only those with a negative or uncertain vaccination history should be tested for VZV IgG. Those with a negative or equivocal result from a qualitative assay require confirmatory testing with a quantitative assay. For immunocompetent pregnant women, a lower cut-off of 100mIU/ml should be used as a marker of previous infection and not 150mIU/ml as for immunosuppressed and neonates.

Recommendation for pregnant contacts

In light of the existing evidence on the safety of aciclovir, the efficacy of aciclovir in preventing clinical chickenpox in healthy and immunosuppressed contacts and the relative sub-optimal efficacy of VZIG as PEP in pregnant women, antivirals are now the treatment of choice for exposure to varicella and shingles for susceptible women exposed in any stage of pregnancy.

All pregnant women who are exposed to chickenpox/ shingles should be assessed for susceptibility as described in section B.3. If there is a previous history of chickenpox in the pregnant woman, she can be re-assured and no PEP is required. If there is no or unknown previous history of chickenpox in the pregnant woman, test for the presence of varicella antibodies. For susceptible women (quantitative assay <100mIU/ml), aciclovir (800mg 4 times a day from days 7 to 14 after exposure) is recommended. Oral valaciclovir 1,000mg 3 times a day can be used as a suitable alternative. VZIG should only be offered if the woman is unable to take oral antivirals due to malabsorption or renal toxicity.

The day of exposure is defined as the date of the onset of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s) respectively. If the woman presents later than day 7 after exposure, a 7- day course of antivirals can be started up to day 14 after exposure, if necessary.

Table 3: Risk assessment for pregnant women with a confirmed significant exposure to chickenpox or shingles

History	Testing	Treatment
A history of chickenpox/ shingles OR 2 recorded doses of varicella vaccine.	Do not test.	Assume immune. No need for PEP.
Uncertain or no history of chickenpox/ shingles AND Unknown or negative varicella vaccine history	Test antenatal booking bloods* (if available) for VZV IgG.	If VZV IgG positive – reassure, patient is immune, do not issue PEP. If VZV IgG negative or equivocal on a qualitative assay, retest with a confirmatory quantitative assay. If quantitative assay is ≥100 mIU/ml – reassure, PEP is not indicated. If the result from quantitative testing will not be available within 10 days of exposure, AND the individual is VZV IgG negative (qualitative testing) then treat with antivirals. If the result from quantitative testing will not be available within 10 days of exposure, AND the individual is VZV IgG equivocal (qualitative testing) then PEP is not recommended.

* For women with an uncertain or negative history of chickenpox, antenatal booking bloods should be tested unless there is a recorded chickenpox exposure in this pregnancy, in which case a fresh sample should be taken for testing if the booking sample is negative.

If the result from quantitative testing will not be available within 10 days of exposure, AND the individual is VZV IgG equivocal (qualitative testing) then PEP with antivirals may not be needed, but could still be considered, based on clinical judgement.

Subsequent exposure to chickenpox or shingles during the same pregnancy

Women who have a second exposure during pregnancy, should be risk assessed and have a repeat VZV antibody test given the rates of seroconversion with both VZIG and aciclovir. Given the short half-life of aciclovir or valaciclovir, if there is a second exposure immediately after a course of antivirals, a second risk assessment and course should be given in the same way starting 7 days after the subsequent exposure.

Pregnant women presenting with chickenpox

If a pregnant woman presents with a chickenpox rash, they should be changed to a therapeutic dose (aciclovir 800mg 5 times a day or 1,000mg valaciclovir 3 times a day for 7 days, starting from the day of onset of the rash). If severe chickenpox develops, the woman should be hospitalised and given IV aciclovir.

Refer to the [Viral Rash in Pregnancy](#) (17) guidance for further details.

Inadvertent administration of attenuated chickenpox or shingles vaccine to pregnant women

Both of the currently available chickenpox vaccines (Varilrix® and Varivax®) and the live shingles vaccine (Zostavax®) contain the same live attenuated strain (Oka) of varicella zoster virus. However, the live attenuated shingles vaccine has significantly higher antigen content than the chickenpox vaccine and therefore a risk assessment is required if a pregnant woman is inadvertently vaccinated. There is limited data on women who have been inadvertently vaccinated with the live attenuated shingles vaccine during pregnancy. Therefore, as a precautionary measure, health professionals should undertake a risk assessment, including assessment of immune status similar to that for a natural exposure. Further information on the management of these women is available at [Chickenpox and shingles vaccines: advice for pregnant women](#).

No treatment is needed if the woman inadvertently receives Shingrix (recombinant zoster vaccine) as it is a non-replicating vaccine.

Women who have inadvertently received the chickenpox vaccine can be reassured that no conditions consistent with congenital varicella syndrome have been reported. However, UKHSA continues to monitor reports of women who have inadvertently received the chickenpox vaccine up to 3 months before pregnancy or at any time during pregnancy and whose pregnancy outcomes are known. Women who have been immunised with any chickenpox/ shingles vaccine (including Shingrix) in pregnancy should be reported to [UKHSA Vaccine in Pregnancy Surveillance](#).

Pregnant women who are inadvertently vaccinated with either chickenpox or live attenuated shingles vaccine (Zostavax) should be advised to seek prompt medical advice if they develop a vesicular rash post vaccination.

3. Infants and neonates

Risk assessment

Although infants (under one years old) may be at increased risk of severe chickenpox infection, the risks of life threatening complications are particularly important in neonates in the first week of life. The risk assessment needs to take a number of factors into account including the presence of maternal antibodies, prematurity, timing of exposure, and whether the infant is still hospitalised.

Post-exposure prophylaxis with VZIG is not usually required for neonates born more than 7 days after the onset of maternal chickenpox, or in those whose mothers develop shingles before or after delivery as these neonates will have maternal antibody.

Post-exposure prophylaxis with VZIG is not indicated for neonates (< 7 days old) whose mothers have been exposed during pregnancy and have been found to be VZV IgG negative unless the mother develops chickenpox. In these circumstances, aciclovir for the mother should be considered (see section on pregnant women). VZIG is only indicated for the neonate if they are directly exposed postnatally in the first week of life.

Post-exposure prophylaxis is recommended for:

- Group 1 – neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery – VZIG can be given without VZV IgG antibody testing of the neonate or mother; in addition, prophylactic intravenous aciclovir should also be considered in addition to the VZIG for infants whose mothers develop chickenpox 4 days before to 2 days after delivery as they are at the highest risk of fatal outcome despite VZIG prophylaxis
- Group 2 –
 - VZV antibody-negative infants under one year who have remained in hospital since birth who are born before 28 weeks gestation OR weighed less than 1,000g at birthor
 - VZV antibody-negative infants who have a severe congenital or other underlying condition that requires prolonged intensive or special care during the first year of life
- Group 3 – VZV susceptible neonates exposed to chickenpox/ shingles (other than in the mother) in the first 7 days of life

In infants over the age of 4 weeks (regardless of gestation at birth) oral aciclovir is the recommended PEP, unless contraindicated (renal toxicity or malabsorption). If contraindicated, VZIG should be given.

Determination of immune status for neonates or infants

For infants in Group 2, maternal antibody may not be present despite a positive maternal history of chickenpox due to immaturity of the immune system at birth, or because birth occurred before maternal antibody transfer is likely to have occurred, or due to waning maternal antibodies. In addition, for those infants in Group 2 who have had repeated blood sampling with replacement by packed red cell infusion, maternal history cannot be relied upon. It is therefore recommended that such infants are tested to determine their VZV antibody status in the event of a contact.

For infants in Group 3, VZV antibody testing is not required for mothers or their infants, if the mother has a positive history of chickenpox/ shingles. As antibody levels following vaccination are lower, for infants in Group 3, whose mothers have received varicella vaccine, antibody testing of the mothers (preferred) or infant is recommended. In addition, for infants in Group 3 whose mothers have a negative or uncertain history of chickenpox/ shingles, testing is also recommended. A higher cut off (150mIU/ml) is used to determine need for VZIG for neonates (when testing either mother or infant's bloods) compared to pregnant women. This is because the aim is to try to prevent infection as opposed to attenuating disease complications.

PEP is recommended for VZV antibody-negative neonates or infants, as defined as:

- infants whose mothers are VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay
- infants who are themselves tested and found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay

Table 4: Risk assessment for neonates or infants with a confirmed significant exposure to chickenpox or shingles

Group	Criteria	Testing	Action
1	Neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery	Not required for mother or infant	Administer VZIG within 7 days of delivery OR within 7 days of onset of disease in the mother, whichever is later
2	Infants (<1yr) who have remained in hospital since birth with any one of the following: – born before 28 weeks gestational age OR – weighed less than 1,000g at birth OR – infants who have severe congenital or other underlying condition that require prolonged intensive or special care during the first year of life	Test for VZV antibody status in the infant only	Administer aciclovir if over the age of 4 weeks starting 7 days after exposure. If less than 4 weeks of age, administer VZIG within 7 days if found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay
3	Neonates exposed to chickenpox/ shingles (other than in the mother) in the first 7 days of life.	Test either mother (preferred) or neonate for VZV antibody status for infants whose mothers have a negative or uncertain history of chickenpox/ shingles OR history of previous varicella vaccine	Administer VZIG within 7 days if found to be VZV antibody-negative by a qualitative assay or <150 mIU/ml by a quantitative assay

Plans for hospital discharge

There is no reason to prevent a newborn baby going home if other members of the household have chickenpox and the mother has had chickenpox or is shown to have VZV antibody. If the mother is susceptible, contact with household members with chickenpox should ideally be delayed until the new baby has reached 7 days of age. For further information see p15 of [Guidance on Viral Rash in Pregnancy](#).

Infants in Group 2 who have previously received VZV post-exposure prophylaxis require a new risk assessment if a second exposure occurs whilst they are still in hospital.

Treatment of neonates with varicella

If chickenpox develops despite VZIG, high dose intravenous aciclovir treatment of 20mg/kg every 8 hours for at least 7 days should be started as soon as possible.

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Annexe 1. Immunosuppression definitions

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 (note: this list not exhaustive)
- immunosuppression due to HIV/AIDS with a current CD4 count of below 200 cells/ μ l (aged 5 years or less, with a CD4 count below 500 cells/ μ l.)
- primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (<1,000 lymphocytes/ μ l), including aplastic anaemia, 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)
- persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example common variable immunodeficiency) or secondary to disease or therapy

Individuals on immunosuppressive or immunomodulating therapy including:

- 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 tumour 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 (note: this list is not exhaustive)
- those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for any indication

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; children 1 mg/kg/day) for more than 10 days in the previous month
- long term moderate dose corticosteroids (equivalent to \geq 10mg prednisolone per day or children 0.5 mg/kg/day for more than 4 weeks) in the previous 3 months

- adults on non-biological oral immune modulating drugs for example 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
- children on any dose of non-biological oral immune modulating drugs
- certain combination therapies at individual doses lower than stated above, including those on ≥ 7.5 mg 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 or children 2 mg/kg/day for more than a week) for any reason in the previous month.

Individuals who had received brief immunosuppression (≤ 40 mg prednisolone per day) for an acute episode (for example asthma / chronic obstructive pulmonary disease (COPD) / coronavirus (COVID-19)) and individuals on replacement corticosteroids for adrenal insufficiency are not considered severely immunosuppressed and can be treated with the standard post exposure treatment.

Annexe 2. Membership of VZ expert working group (August 2018 to April 2022)

Chair: Professor Judy Breuer; Professor of Virology University College London, Honorary Consultant Virologist Great Ormond Street Hospital, Previous Chair of the JCVI varicella subcommittee

Ruth Parry (secretariat); Immunisation and Vaccine Preventable Diseases Division, UKHSA

Dr Kevin Brown; Consultant Medical Virologist, Immunisation and Vaccine Preventable Diseases Division; Current Chair of the JCVI varicella subcommittee

Professor Liz Miller; Consultant Epidemiologist, London School of Hygiene and Tropical Medicine

Professor Adam Finn; Professor of Paediatrics, Schools of Cellular and Molecular Medicine and of Population Health Sciences, University of Bristol

Professor Asma Khalil; Professor of Maternal Fetal Medicine, Fetal Medicine Unit, Department of Obstetrics and Gynaecology, St George's University of London, St. George's Hospital

Dr Philip Rice; Consultant Medical Virologist, Norfolk and Norwich University Hospitals NHS Foundation Trust*

Professor Mary Ramsay, Director of Public Health Programmes (including Immunisation), UKHSA

Dr Gayatri Amirthalingam; Deputy Director of Immunisation and Vaccine Preventable Diseases Division, UKHSA

Professor Paul Heath; Professor of Paediatric Infectious Diseases, St George's University Hospitals NHS Foundation Trust

Dr Jessica Bate, Consultant Paediatric Oncologist and Honorary Senior Clinical Lecturer, University Hospital Southampton

Sharon Webb: NHS infectious diseases in pregnancy programme manager, PHE Screening*

Alan Russell; Senior Principal Pharmacist and Associate Commercial Specialist, Vaccine and Medical Countermeasures, Commercial Directorate, Department of Health and Social Care*

*Members of expert working group between August 2018 to April 2020

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