VIRAL SKIN INFECTIONS

CHI Formulary Indication Review

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Council of Health Insurance

INDICATION UPDATE

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ADDENDUM to the CHI Original Viral Skin Infections Clinical Guidance - Issued April 2020

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Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

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Abbreviations

AAFP	American Academy of Family Physicians
AAHKS	American Association of Hip and Knee Surgeons
AAOS	American Academy of Orthopaedic Surgeons
ACR	American College of Rheumatology
AGIHO	Arbeitsgemeinschaft Internistische Onkologie (German Working Group on Internal Oncology)
AIDS	Acquired Immunodeficiency Syndrome
CDC	Centers for Disease Control and Prevention
CHI	Council of Health Insurance
CNS	Central Nervous System
DGHO	Deutsche Gesellschaft für Hämatologie und Medizinische Onkologie (German Society for Hematology and Medical Oncology)
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
HNSCC	Head and Neck Squamous Cell Carcinoma
HPV	Human Papillomavirus
HSCT	Hematopoietic Stem Cell Transplantation
HSV	Herpes Simplex Virus
IV	Intravenous
MC	Molluscum Contagiosum
MMR	Measles, Mumps, Rubella (vaccine)
MSM	Men Who Have Sex with Men
NHSGGC	NHS Greater Glasgow and Clyde
NSAIDS	Nonsteroidal Anti-Inflammatory Drugs
PE	Prescribing Edits
PEP	Post-Exposure Prophylaxis
SFDA	Saudi Food and Drug Authority
STI	Sexually Transmitted Infection
UK	United Kingdom
VZIG	Varicella Zoster Immune Globulin
VZV	Varicella Zoster Virus
WHO	World Health Organization

Executive Summary

Viral skin infections are conditions caused by the invasion and replication of viruses within the skin. These infections can affect various layers of the skin, including the epidermis (outer layer) and sometimes the dermis (deeper layer). Viruses that cause skin infections include a variety of families, such as herpesviruses, poxviruses, and papillomaviruses[1].

The presentation of viral skin infections can vary widely, ranging from characteristic lesions like vesicles, pustules, or warts to more general symptoms such as itching, redness, and inflammation. Some viral skin infections are highly contagious and can be transmitted through direct contact with infected individuals or contaminated objects. Here is a list of common signs and symptoms accompanying viral skin infections:

- **Lesions or Bumps:** Most viral skin infections are characterized by the presence of specific skin lesions, such as vesicles (fluid-filled sacs), pustules (pus-filled lesions), or warts.
- **Redness and Inflammation**
- **Itching or Pain:** in some cases, there may be pain or tenderness associated with the lesions.
- **Rash:** Many viral skin infections present with a rash, which can vary in appearance depending on the specific virus involved.
- **Ulcers or Sores:** Some viral infections may lead to the formation of ulcers or open sores on the skin.
- **Fever:** Systemic symptoms such as fever can accompany certain viral skin infections, especially during the initial stages[2].

Viral Skin Infections can be categorized into the following types based on the microorganism causing the infection:

- **Herpes Simplex Virus (HSV) Infections:**
  - HSV-1: Typically causes oral herpes, including cold sores.
  - HSV-2: Primarily responsible for genital herpes.
- **Varicella-Zoster Virus (VZV) Infection:**
  - Causes chickenpox (varicella) and later can re-emerge as shingles (herpes zoster).

- **Human Papillomavirus (HPV) Infections:**
  - Responsible for various skin conditions, including warts and some types of skin cancer.
- **Poxvirus Infections:**
  - Examples include molluscum contagiosum, a viral skin infection characterized by small, flesh-colored bumps[1].

Several risk factors can increase an individual's likelihood of developing Viral Skin Infections. These risk factors include:

- Being in close contact with an infected individual or their lesions increases the risk of transmission.
- Individuals with weakened immune systems, due to conditions like HIV/AIDS or immunosuppressive medications, are more susceptible to viral skin infections.
- Children and older adults may be more vulnerable to certain viral skin infections.
- Open wounds or breaks in the skin can provide entry points for viruses, increasing the risk of infection.
- Lack of proper hygiene practices may contribute to the spread of certain viral infections[3].

Some of the complications and related problems associated with Viral Skin Infections include:

- **Secondary Bacterial Infection:** Scratching the affected area may introduce bacteria, leading to a secondary bacterial infection.
- **Scarring**: Some viral skin infections, especially those causing deep lesions, may result in scarring.
- **Dissemination:** In some cases, the virus may spread beyond the initial site of infection, leading to more widespread or severe symptoms.
- **Neurological Complications:** In conditions like shingles, there is a risk of neurological complications, such as postherpetic neuralgia.
- **Recurrence:** Certain viral skin infections, such as herpes simplex, can recur periodically[2].

Viral skin infections frequently lead individuals to seek medical attention and pose significant global public health challenges. Vaccines designed to combat viral diseases with notable skin-related effects, such as measles and rubella (administered in conjunction with a mumps vaccine as the trivalent MMR), human papillomavirus,

varicella, and zoster, have proven effective. Despite the success of vaccination in preventing these diseases, comprehensive epidemiological data on their prevalence and distribution at a large scale are still limited[4].

The literature on the patterns of general and specific skin diseases is scanty, and only a few published reports are available on Saudi Arabia. Though community-based studies are the best to determine the incidence of a particular disease, they are difficult to carry out. As such, most of the studies to determine the incidence or prevalence of dermatological diseases are based upon hospital attendees. The study included 3051 patients comprising 1786 (58.5%) males and 1265 (41.5%) females. Males outnumbered females. The mean age (standard error of the mean) of the patients was 25.3 (0.27) years. About 71% of the patients were between 5 and 34 years of age. The top five skin diseases were eczema/ dermatitis (19.5%), viral infections (16.6%), pilosebaceous disorders (14.4%), pigmentary lesions (11.2%) and hair disorders (7.6%). The major disorder in males was viral skin infections (20.0%), while eczema/dermatitis (20.7%) constituted the most prevalent skin disease in females. Seasonal variations were recorded in cases of pigmentary lesions, papulosquamous disorders and protozoal infections[5].

The burden of disease associated with viral skin infections is a substantial concern in public health. These infections contribute significantly to the overall morbidity and healthcare burden globally. A study evaluated the disease burden of viral skin infections that was assessed as a function of gross-domestic product (GDP). The increase in disease burden with increased GDP may be correlated to decreased access to dermatologists in developing countries. An increased burden with infections is likely due to skin barrier and immune regulatory dysfunction. The morbidity of skin diseases demonstrates the need for increased access to vaccination campaigns and dermatologic care across developing nations[6].

Drug therapy is an integral component for the management of viral skin infections. The goals of treating Viral Skin Infections depend on its underlying cause and the individual's specific needs and health condition. However, common goals of treatment include relieving symptoms, reducing viral replication, preventing complications, accelerating healing, preventing transmission and recurrence, and improving quality of life[2].

Treatment for viral skin infections typically involves a combination of approaches, including non-pharmacological interventions and pharmacological interventions.

Treatment of viral skin infections varies depending on the specific virus involved. Here are general approaches for some common viral skin infections:

- **Antiviral Medications:**

- *Herpes Simplex Virus (HSV):* Antiviral medications such as acyclovir, valacyclovir, and famciclovir are commonly prescribed to reduce the severity and duration of symptoms during outbreaks of oral or genital herpes.
- *Varicella-Zoster Virus (VZV):* Antiviral drugs, including acyclovir, valacyclovir, and famciclovir, can be used to treat chickenpox and shingles.

- **Topical Treatments:**
  - *Molluscum Contagiosum:* Lesions can be treated with cryotherapy (freezing), curettage (scraping), or topical agents like cantharidin.
- **Pain Management:**
  - For viral infections causing pain, over-the-counter pain relievers like acetaminophen or ibuprofen may be recommended.
- **Antiviral Creams:**
  - *Human Papillomavirus (HPV):* Topical treatments like imiquimod or podophyllotoxin may be used for certain types of warts caused by HPV.
- **Vaccination:**
  - Prevention is crucial. Vaccines are available for viruses causing some skin infections, such as the varicella vaccine for chickenpox and the human papillomavirus (HPV) vaccine for certain HPV-related conditions.
- **Supportive Care:**
  - Adequate hydration, rest, and maintaining good overall health can help the body combat the viral infection.
- **Avoiding Spreading the Infection:**
  - Practicing good hygiene, such as regular handwashing, and avoiding close contact with others can prevent the spread of viral skin infections.
- **Immune Support:**
  - Maintaining a healthy immune system through a balanced diet, regular exercise, and sufficient sleep can aid in the body's ability to fight viral infections[2].

CHI issued Viral Skin Infections clinical guidance after thorough review of renowned international and national clinical guidelines in April 2020. Updating

clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Viral Skin Infections clinical guidance and seeks to offer guidance for the effective management of Viral Skin Infections. It provides an **update on the Viral Skin Infections Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of updated versions of previously reviewed guidelines** namely CDC Chickenpox (Varicella) Treatment Guidelines **(2022).**

Moreover, **new guidelines are added to the report** such as:

- CDC; Preventing Varicella-Zoster Virus (VZV) Transmission from Herpes Zoster in Healthcare Settings (**2023**)
- NHS Clinical Guideline for the Management of Varicella-Zoster (VZV) Infections to prevent nosocomial Transmission to at-risk individuals (**2023**)
- UK Health Security Agency; Guidelines on post exposure prophylaxis (PEP) for varicella or shingles (**2023**)
- Management of herpesvirus reactivations in patients with solid tumors and hematologic malignancies: update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) on herpes simplex virus type 1, herpes simplex virus type 2, and varicella zoster virus (**2022**)
- NHSGGC Pediatrics for Health Professionals; Varicella Zoster Infection (chickenpox): management in children (**2022**)
- Review Article: Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment (*Clinical, Cosmetic and Investigational Dermatology*, **2019**)
- Guidelines for the Treatment of Measles by Centers for Disease Control and Prevention (CDC) of America – November 5, **2020**.

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there has been **no withdrawal** of drugs. Moreover, there have been **no newly approved drugs** for the treatment of Viral Skin Infections.

Additionally, there have been **updates** regarding previously mentioned drugs in terms of drug information and prescribing edits since April 2020.

Table 1. Prescribing Edits (PE) Modifications for Viral Skin Infections Medications

Drugs	PE modifications
FAMCICLOVIR for chickenpox (varicella)	Add ST: famciclovir is generally not the first-line treatment for uncomplicated chickenpox, especially in healthy individuals. The preferred antiviral medications for chickenpox are acyclovir and valacyclovir.
FAMCICLOVIR for herpes simplex virus (herpes labialis)	Add ST: famciclovir is not typically considered a first-line treatment for herpes labialis (cold sores) caused by the herpes simplex virus (HSV). First-line treatments usually include medications like acyclovir and valacyclovir.
FAMCICLOVIR for herpes zoster (shingles)	Add ST: famciclovir is generally not the first-line treatment for zoster.
PODOPHYLLOTOXIN	Add AGE: not to be used in children < 12 years of age.
VARICELLA ZOSTER VIRUS GLYCOPROTEIN E ADJUVANTED WITH AS01B	Add AGE: zoster vaccine is not a substitute for varicella vaccine and should not be used in children and adolescents.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the viral skin infections therapeutic management.

Below is a table summarizing the major changes based on the different Viral Skin Infections guidelines used to issue this report:

Table 2. General Recommendations for the Management of Viral Skin Infections

Management of Viral Skin Infections		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
Managing People at High Risk for Severe Varicella: *Varicella-Zoster Immune Globulin* Recommend VariZIG™ for individuals unable to receive the varicella vaccine, particularly those lacking evidence of	Not graded[7]	CDC[7]

immunity, facing probable infection due to exposure, or at high risk for severe varicella. Administer promptly after exposure to varicella-zoster virus (VZV) preferably within 10 days of exposure.		
Managing People at High Risk for Severe Varicella: *Acyclovir Treatment* Recommend oral acyclovir or valacyclovir treatment for high-risk groups, including healthy individuals above 12 years old, those with chronic cutaneous or pulmonary disorders, and individuals receiving certain therapies. Administer oral therapy within 24 hours after the onset of varicella rash for maximum effectiveness. **Intravenous acyclovir therapy is recommended for severe disease (e.g., disseminated VZV such as pneumonia, encephalitis, thrombocytopenia, severe hepatitis) and for varicella in immunocompromised patients (including patients being treated with high-dose corticosteroid therapy for >14 days). It is recommended for the pregnant patient with serious, viral-mediated complications of varicella, such as pneumonia.** Famciclovir is not established for children; use Foscarnet for acyclovir-resistant VZV strains, consulting an infectious disease specialist.	Not graded[7]	CDC[7]
Assessing Immunity to Varicella: Administer two doses of varicella vaccine for all individuals without evidence of immunity. Individuals with no epidemiologic link or laboratory confirmation of varicella should receive a second vaccine dose.	Not graded[7]	CDC[7]

Chickenpox treatment o Administration of Varicella Zoster Immunoglobulin (VZIG) can prolong incubation period to 28 days. o There is no role for VZIG in the management of acute cases of chickenpox. o Use of high dose acyclovir should be considered early in infection for adults and immunocompromised patients.	Not graded[8]	NHS[8]
Shingles treatment o If required is with either oral or intravenous acyclovir depending on disease severity and underlying health conditions.	Not graded[8]	NHS[8]
VZV post exposure prophylaxis (PEP) is recommended for individuals who fulfil all the following criteria: o significant exposure to chickenpox (varicella) or shingles (zoster) during the infectious period o at increased risk of severe chickenpox such as immunosuppressed individuals, neonates, and pregnant women o no antibodies to VZV – urgent VZV antibody testing can be performed within 24 hours	Not graded[9]	UKHSA[9]
Types of VZV PEP: *Oral acyclovir* o Oral acyclovir (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. o Individuals in these groups who are exposed to chickenpox or shingles	Not graded[9]	UKHSA[9]

should be assessed and for those identified as susceptible antivirals (oral acyclovir or valaciclovir) should be given from day 7 to day 14 after exposure.		
Types of VZV PEP: *VZIG* o 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. o VZIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts) of the day of exposure	Not graded[9]	UKHSA[9]
Types of VZV PEP: *IVIG* o Contacts with bleeding disorders who cannot receive antivirals or be given an intramuscular injection should be given intravenous human normal intravenous 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. o IVIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts)	Not graded[9]	UKHSA[9]
VZV in pregnant women Immunocompetent pregnant women with a confirmed history of previous VZV infection or immunization are considered immune, requiring no further action following exposure.	Not graded[8] [9]	NHS[8] [9]

Pregnant women without such a history should undergo testing for VZV IgG during booking blood, and if the result is negative, post-exposure prophylaxis is recommended throughout pregnancy. If exposure occurs in the first 20 weeks, VZIG prophylaxis is advised, while exposures after 20 weeks allow for a choice between VZIG and acyclovir, considering patient and healthcare professional preferences and the ability to administer timely prophylaxis (VZIG offered if the woman is unable to take oral antivirals due to malabsorption or renal toxicity).		
VZV in pregnant women For susceptible women, acyclovir (800 mg 4 times/day from days 7 to 14 after exposure) is recommended. Oral valaciclovir 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.	Not graded[9]	UKHSA[9]
VZV in neonates VZV post-exposure prophylaxis for neonates is with VZIG. Situations in which this is indicated include: o Neonates, whose mothers have developed chickenpox (not shingles) in the period 7 days before to 7 days after delivery. o Neonates 7 days old or less in contact with chickenpox or shingles whose mothers have no history of chickenpox and have no antibody. o VZV IgG negative infants in the first year of life, exposed to chickenpox or shingles whilst still undergoing	Not graded[8] Not graded[9] Not graded[10]	NHS[8] UKHSA[9] NHSGGC[10]

prolonged or intensive special care nursing. o VZV IgG negative infants under 1 year old who have remained in hospital since birth and were born before 28 weeks gestation, or who weighed less than 1000g at birth. For very high-risk exposures, acyclovir may be required in addition to VZIG- discuss with virology.		
VZV in children o In immunocompetent children aged over 1 month and in good health, antiviral treatment is typically unnecessary. o For at-risk children with the potential for moderate disease, consider oral Acyclovir for a duration of FIVE days. o Consider IV acyclovir for severe varicella in children not previously identified as immunodeficient, as this could indicate severe immune compromise.	Not graded[10]	NHSGGC[10]
VZV in children symptomatic treatment o Paracetamol for fever o Topical calamine can be used but there is no evidence basis, and it can be felt to dry the skin and increase itching. o Antihistamines (e.g., chlorphenamine) can be used for itching. o **NSAIDS (e.g., Ibuprofen) should be avoided**	Not graded[10]	NHSGGC[10]
PEP in children o Both varicella-zoster immunoglobulin (VZIG) and oral acyclovir are suitable for prophylaxis	Not graded[10]	NHSGGC[10]

○ If there's no known history of chickenpox, prophylaxis should be administered from day 7 to day 14 post-exposure. ○ For patients presenting after day 7 of exposure, a 7-day antiviral course can begin as soon as possible and extend up to day 14 post-exposure if needed. ○ In situations where concerns exist about malabsorption or oral antivirals are contraindicated, VZIG should be considered and administered as soon as possible within 7 days of exposure. For patients presenting after 7 days, there may still be a benefit in giving VZIG up to 10 days post-exposure. Varicella antibodies should be checked, and VZIG should only be given if negative or the result is <150mIU/ml.		
Management of Patients with Varicella-Zoster Infection: ○ Patients with VZV infection must be isolated immediately in single rooms with closed doors and with no contact with persons without evidence of immunity, this must include visitors and healthcare workers. ○ Respiratory precautions (chickenpox) and contact precautions (shingles) must be adhered to until all lesions are dry and crusted. ○ The patient should be isolated until all the skin lesions are crusted which is usually about four to seven days after the appearance of the rash.	Not graded[8]	NHS[8]

Management of Healthcare Personnel with Herpes Zoster o For localized herpes zoster in an immunocompetent person - Cover lesions and restrict from care of high-risk patients (i.e., patients who are susceptible to varicella and at increased risk for complications of varicella, including neonates, pregnant women, and immunocompromised persons of any age) until all lesions are dry and scabbed. - If lesions cannot be completely covered, exclude from duty until all lesions are dry and scabbed.	Not graded[11]	CDC[11]
Management of Healthcare Personnel Exposed to Someone with Herpes Zoster (one or more documented doses of the varicella vaccine or proof of varicella immunity): o Do not require post-exposure prophylaxis and face no work restrictions. o Ensure up-to-date immunization with two documented doses of the varicella vaccine. • If only one documented dose has been received, the second dose should be administered within 3 to 5 days after exposure, provided at least 4 weeks have passed since the first dose.	Not graded[11]	CDC[11]
Management of Healthcare Personnel Exposed to Someone with Herpes Zoster (without documented vaccination or evidence of varicella immunity):	Not graded[11]	CDC[11]

○ Should be furloughed or temporarily reassigned to locations distant from patient-care areas during this period. ○ Should receive post-exposure vaccination: • recommended within 3 to 5 days of exposure to the rash. It remains effective even if administered 6 or more days after exposure, providing protection against subsequent exposures if the current exposure did not result in infection. ○ Varicella zoster immune globulin is advised if at risk for severe disease and varicella vaccination is contraindicated, such as in pregnant healthcare personnel.		
HSV/VZV prophylaxis for immunocompromised: ○ Acyclovir has long been the primary choice for prophylaxis and treatment of HSV (herpes simplex virus) and VZV (varicella-zoster virus) in immunocompromised patients. ○ Recommendations include oral acyclovir 400 mg BID or 400 mg QID as prophylaxis for oral HSV disease. ○ Oral acyclovir is recommended to reduce clinical VZV reactivation; dosages from 400 mg once daily to 400 mg TID have been shown to be efective. ○ Oral valacyclovir can be an alternative for oral HSV, but the best regimen (250 mg BID or 500 mg BID) has not yet been defined.	AIIr[12] for acyclovir BI[12] for valacyclovir	AGIHO/DGHO[12]

○ For patients not tolerating oral medication, intravenous acyclovir 250 mg/m2 TID is suitable for oral HSV.		
HSV/VZV prophylaxis for immunocompromised: Antiviral prophylaxis with acyclovir is standard of care in allogeneic and autologous HSCT recipients and non-HSCT patients undergoing tumor treatment. Recommendations include oral acyclovir to reduce clinical VZV reactivation, with dosages ranging from 400 mg once daily to 400 mg TID	AII[12]	AGIHO/DGHO[12]
Vaccination in immunocompromised individuals: Highly effective vaccines, including the live-attenuated varicella virus (vOKA) for primary prophylaxis against varicella-zoster virus (VZV), are available. Two herpes zoster vaccines, Zostavax® and Shingrix®, have been approved, with Shingrix® preferred for immunocompromised individuals. Shingrix® is recommended for adults aged 50 or older and those at increased risk of herpes zoster, despite limited long-term data. For high-risk groups like those with hematologic malignancies, considering additional acyclovir prophylaxis is suggested until more comprehensive data, especially from comparative trials, become available.	Not graded[12]	AGIHO/DGHO[12]
The decision to initiate treatment for (HSV) or (VZV) reactivation is based on clinical diagnosis, preceding confirmation	Not graded[12]	AGIHO/DGHO[12]

through virus detection. Oral administration is suitable for localized diseases with minor symptoms and mild immunosuppression, with acyclovir, valacyclovir, and famciclovir. Duration of therapy: 7 to 10 days, with close clinical monitoring. Intravenous acyclovir is recommended for severe cases, especially for patients with high immunosuppression and a risk of complications. Treatment duration for disseminated, cerebral, or visceral disease is at least 14 days. Treatment recommendations for patients with malignancies generally align with those for the general population.		
Molluscum Contagiosum (MC) Treatment: Consensus recommends treatment for extensive disease, secondary complications (bacterial superinfection, molluscum dermatitis, conjunctivitis), or aesthetic concerns. General preventive measures for all patients include avoiding scratching, rubbing lesions, and sharing personal items.	Not graded[13]	Meza-Romero et al. (2019)[13]
Active treatments are categorized into mechanical, chemical, immunomodulatory, and antiviral methods. Mechanical methods such as cryotherapy and curettage show efficacy, but drawbacks include potential blistering, scarring, and pigmentation changes. Chemical methods like cantharidin and potassium hydroxide exhibit variable cure rates, with caution in specific regions due to infection risks. Immunomodulatory methods, including imiquimod, oral cimetidine, interferon alfa, candidin, and diphencyprone, present mixed efficacy and controversies. Antivirals like cidofovir, used in immunosuppressed patients, can be administered topically or	Not graded[13]	Meza-Romero et al. (2019)[13]

intravenously, with the latter carrying nephrotoxicity risks.		
Measles treatment: Measles treatment does not involve specific antiviral therapy but focuses on supportive medical care to alleviate symptoms and manage complications, especially bacterial infections. Severe cases in hospitalized children may require vitamin A treatment, with recommended daily doses based on age.	Not graded[14]	CDC[14]
Measles post-exposure Prophylaxis: PEP is recommended for those exposed to measles without prompt immunity demonstration. MMR vaccine or immunoglobulin (IG) should be administered within specified time frames to potentially offer protection.	Not graded[14]	CDC[14]
Isolation: o Infected individuals should be isolated for four days after the rash onset, with strict airborne precautions in healthcare settings. o Healthcare providers caring for measles patients should observe airborne precautions, with preferred placement in a single-patient airborne infection isolation room (AIIR). o Regardless of immunity status, healthcare staff should use respiratory protection like an N95 respirator when entering the room to prevent airborne transmission.	Not graded[14]	CDC[14]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Viral Skin Infections clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts; the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Viral Skin Infections report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

The following segment contains the updated versions of the guidelines mentioned in the April 2020 CHI Viral Skin Infections Report and the corresponding recommendations:

Table 3. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
1.1 AAFP Herpes Zoster and Postherpetic Neuralgia: Prevention and Management (2017)	N/A*
1.2 AAFP Nongenital Herpes Simplex Virus (2010)	N/A*
1.3 CDC Chickenpox (Varicella) Treatment Guidelines (not dated)	CDC Chickenpox (Varicella) Treatment Guidelines (**2022**)

**N/A: not available (no new updates for those guidelines)*

1.1.1 Centers for Disease Control and Prevention (CDC) Chickenpox (Varicella) Treatment Guidelines (2022)

The CDC has issued recommendations below[7]:

People at High Risk for Severe Varicella

- Immunocompromised individuals lacking proof of immunity to varicella, such as:
  - Individuals diagnosed with leukemia or lymphoma;
  - Individuals using immune system-suppressing medications like high-dose systemic steroids or chemotherapeutic agents;

        - Individuals with cellular immune deficiencies or other issues with their immune system.
    - Newborns born to mothers with varicella within five days before to two days after delivery.
    - Premature infants exposed to varicella or herpes zoster, specifically:
        - Hospitalized premature infants born at 28 weeks of gestation or later, with mothers lacking evidence of immunity;
        - Hospitalized premature infants born at less than 28 weeks of gestation or weighing ≤1,000 grams at birth, regardless of their mothers' varicella immunity status.
    - Pregnant women lacking evidence of immunity to varicella.

Managing People at High Risk for Severe Varicella

Recommendations for Varicella-Zoster Immune Globulin:

- For individuals exposed to varicella or herpes zoster unable to receive the varicella vaccine, consider varicella-zoster immune globulin (VariZIG™) to prevent the development or reduce the severity of varicella. This is particularly advisable for those who:
    - Lack evidence of immunity to varicella.
    - Face a probable infection due to exposure.
    - Are at high risk for severe varicella.
- Administer VariZIG™ promptly after exposure to varicella-zoster virus (VZV), preferably within 10 days of exposure.

Recommendations for Acyclovir Treatment:

- Consider oral acyclovir or valacyclovir treatment for the following high-risk groups at increased risk for moderate to severe varicella:
    - Healthy individuals above 12 years old.
    - Individuals with chronic cutaneous or pulmonary disorders.
    - Those receiving long-term salicylate therapy.
    - Individuals receiving short, intermittent, or aerosolized courses of corticosteroids.

- Healthcare providers may opt for oral acyclovir or valacyclovir for secondary cases within a household. Administer oral therapy within the first 24 hours after the onset of the varicella rash for maximum effectiveness. However, AAP does not recommend oral acyclovir or valacyclovir for otherwise healthy children experiencing typical varicella without complications.
- For pregnant women with varicella, especially in the second and third trimesters, some experts recommend oral acyclovir or valacyclovir. Intravenous acyclovir is advised for pregnant patients with serious viral-mediated complications, such as pneumonia.
- Intravenous acyclovir therapy is recommended for severe disease (e.g., disseminated VZV, pneumonia, encephalitis, thrombocytopenia, severe hepatitis) and for varicella in immunocompromised patients (including those on high-dose corticosteroid therapy for >14 days).
- While Famciclovir is available for treating VZV infections in adults, its efficacy and safety have not been established for children. In cases of infections caused by acyclovir-resistant VZV strains, typically occurring in immunocompromised individuals, Foscarnet should be used, with consultation from an infectious disease specialist recommended.

Assessing immunity to Varicella

- Two doses of varicella vaccine are recommended for all children, adolescents, and adults without evidence of immunity to varicella. Those who previously received one dose of varicella vaccine should receive their second dose for best protection against the disease.
- People who have neither an epidemiologic link nor laboratory confirmation of varicella should not be considered as having a valid history of disease. For these people, a second dose of vaccine is recommended if they previously received only one dose. If a healthcare provider verifies the diagnosis based on the above criteria, then vaccination is not needed.

1.2 Additional Guidelines

This part includes the added guidelines to the previous CHI Viral Skin Infections report, along with their recommendations.

Table 4. List of Additional Guidelines

Additional Guidelines
Centers for Disease Control and Prevention (CDC) Preventing Varicella-Zoster Virus (VZV) Transmission from Herpes Zoster in Healthcare Settings **(2023)**
NHS Clinical Guideline for the Management of Varicella-Zoster (VZV) Infections to prevent nosocomial Transmission to at-risk individuals **(2023)**
UK Health Security Agency; Guidelines on post exposure prophylaxis (PEP) for varicella or shingles **(2023)**
Management of herpesvirus reactivations in patients with solid tumors and hematologic malignancies: update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) on herpes simplex virus type 1, herpes simplex virus type 2, and varicella zoster virus **(2022)**
NHSGGC Pediatrics for Health Professionals; Varicella Zoster Infection (chickenpox): management in children **(2022)**
Review: Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment (Clinical, Cosmetic and Investigational Dermatology, **2019**)
Guidelines for the Treatment of Measles by Centers for Disease Control and Prevention of America – November 5, **2020**

1.2.1 Centers for Disease Control and Prevention (CDC) Preventing Varicella-Zoster Virus (VZV) Transmission from Herpes Zoster in Healthcare Settings (2023)

The CDC has issued recommendations below[11]:

Preventing Varicella in Healthcare Settings; Nosocomial Transmission of VZV

- Nosocomial transmission of VZV is well-recognized and can be life threatening to certain groups of patients.
- Patients, healthcare providers, and visitors with varicella or herpes zoster can spread VZV to susceptible patients and healthcare providers in hospitals, long-term-care facilities, and other healthcare settings. In healthcare settings, transmissions have been attributed to delays in the diagnosis or reporting of varicella and herpes zoster and failures to implement control measures promptly.

Management of Patients with Herpes Zoster

- The approach to infection control is contingent upon the patient's immune status (immunocompetent or immunocompromised) and the extent of the rash, whether it is confined or disseminated (lesions present beyond the primary or neighboring dermatomes).
- Irrespective of these factors, adhere to standard infection control measures. Refer to the table below to ascertain if supplementary infection control precautions are necessary.

Table 5. Infection Control Precautions Based on Patient's Immune Status and Rash Localization

Patient Immune Status	Localized Herpes Zoster	Disseminated Herpes Zoster
Immunocompetent	Completely cover lesions and follow standard precautions until lesions are dry and scabbed.	Airborne and contact precautions until lesions are dry and scabbed.
Immunocompromised	Airborne and contact precautions until disseminated infection is ruled out. After dissemination is ruled out, completely cover lesions, and follow standard precautions until lesions are dry and scabbed.	Airborne and contact precautions until lesions are dry and scabbed.

Management of Healthcare Personnel with Herpes Zoster

- For localized herpes zoster in an immunocompetent person
  - Cover lesions and restrict from care of high-risk patients (i.e., patients who are susceptible to varicella and at increased risk for complications of varicella, including neonates, pregnant women, and immunocompromised persons of any age) until all lesions are dry and scabbed.
  - If lesions cannot be completely covered, exclude from duty until all lesions are dry and scabbed.
- For disseminated herpes zoster or localized herpes zoster in an immunocompromised person until disseminated infection is ruled out: exclude from duty until all lesions are dry and scabbed.

Management of Healthcare Personnel Exposed to Someone with Herpes Zoster

1. **Healthcare personnel with one or more documented doses of the varicella vaccine or proof of varicella immunity:**

- Do not require post-exposure prophylaxis and face no work restrictions.
- Ensure up-to-date immunization with two documented doses of the varicella vaccine.
    - If only one documented dose has been received, the second dose should be administered within 3 to 5 days after exposure, provided at least 4 weeks have passed since the first dose.
- **Practice self-monitoring or have the employee health program or an infection control nurse monitor** from the 8th day after the initial exposure through the 21st day after the last exposure. **Promptly report any symptoms such as fever, headache, skin lesions, or systemic issues.**
    - If symptoms manifest, healthcare personnel should be promptly removed from patient care, placed on sick leave, and provided with antiviral medication.

2. **Healthcare personnel without documented vaccination or evidence of varicella immunity:**

- Are considered susceptible to varicella-zoster virus (VZV) infection.
- **May be potentially infectious** from the 8th day after the first exposure through the 21st day after the last exposure.
- **Should be furloughed or temporarily reassigned** to locations distant from patient-care areas during this period.
- **Should receive post-exposure vaccination** following guidelines from the Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC).
    - Vaccination is recommended within 3 to 5 days of exposure to the rash. It remains effective even if administered 6 or more days after exposure, providing protection against subsequent exposures if the current exposure did not result in infection.
- **Varicella zoster immune globulin** is advised if at risk for severe disease and varicella vaccination is contraindicated, such as in pregnant healthcare personnel.
    - If varicella zoster immune globulin is used as post-exposure prophylaxis, the individual should be excluded from work from the 8th

day after the first exposure through the 28th day after the last exposure.

Recommendations for healthcare institutions to prevent varicella and nosocomial spread

- Have documented evidence of varicella immunity for all healthcare personnel readily available at the healthcare personnel's work location.
- Alert healthcare personnel without evidence of immunity to varicella about the risks of possible infection and offer those without evidence of immunity two doses of varicella vaccine, administered 4 to 8 weeks apart, when they begin employment.
- Establish protocols and recommendations for screening and vaccinating healthcare personnel and for managing healthcare personnel after exposures in the workplace.

1.2.2 National Health Service (NHS) Clinical Guideline for the Management of Varicella-Zoster (VZV) Infections to Prevent Nosocomial Transmission to At-Risk Individuals (2023)

The NHS has issued recommendations below[8]:

Chickenpox

Treatment

- Incubation period is generally between 10 - 21 days, but usually 14 days. Administration of Varicella Zoster Immunoglobulin (VZIG) can prolong incubation period to 28 days.
- There is no role for VZIG in the management of acute cases of chickenpox.
- Use of high dose acyclovir should be considered early in infection for adults and immunocompromised patients.

Isolation

- Person to person transmission occurs by direct contact, droplet, and airborne spread of secretions from the respiratory tract or vesicles. The virus can be spread indirectly on hands and inanimate objects.
- Respiratory isolation procedures are required i.e. a single room with use of gloves, aprons, masks, and attention to hand hygiene to prevent infection of non-immune staff and susceptible patients.
- Patients with chickenpox should be cared for by immune staff only.

Shingles

- Shingles are less contagious (there is no infectious incubation period) as the virus is confined to a rash which can be covered in most cases. Nonimmune patients are at risk of contracting chickenpox from patients with shingles.
- Those who have had chickenpox who come into contact with a person with shingles are not at risk of acquiring the disease as they will be immune.

Isolation

- Person to person transmission is via direct contact with the rash or from spread of secretions from the rash to non-immune persons.
- Contact isolation procedures are required i.e. single room with use of gloves and apron and attention to hand hygiene to prevent infection of non-immune staff and transfer of virus to susceptible patients.

Treatment

- If required is with either oral or intravenous acyclovir depending on disease severity and underlying health conditions.

Management of Patients with Varicella-Zoster Infection

- In the event of an infection with VZV occurring in hospital the following actions must be taken: patients with VZV infection must be isolated immediately in single rooms with closed doors and with no contact with persons without evidence of immunity, this must include visitors and healthcare workers.
- Suspicion of VZV infection should be confirmed by sending a green viral swab of a lesion(s) for PCR.
- Respiratory precautions (chickenpox) and contact precautions (shingles) must be adhered to until all lesions are dry and crusted.
- The patient must be nursed in a side room with designated toilet facilities.
- Respiratory (chickenpox) and contact (shingles) precautions posters applied.
- Patients do not need to be nursed in negative pressure rooms.
- The patient should be isolated until all the skin lesions are crusted which is usually about four to seven days after the appearance of the rash.
- Offer patient chickenpox/shingles information leaflet.
- Nonimmune patients who have been exposed to the patient with Varicella Zoster infection and who are still in hospital should be isolated from 7 days following their first exposure until 21 days after their last exposure. This period

is extended by 7 days if post-exposure prophylaxis is given because this can prolong the incubation period.

Personnel Protective Equipment (PPE)

- During the period of isolation, appropriate PPE must be worn for direct patient contact reflecting respiratory or contact precautions as required.
- Hands must be decontaminated after the removal of gloves. Strict compliance with hand washing techniques must be observed at all times.
- Eye protection should be considered dependent on the care activity being performed. Disposal of clinical waste
- All waste from the room should be disposed of as clinical waste for the duration that the patient is in isolation.

Cutlery/Crockery

- Normal ward issue can be used but must be cleaned by washing in a dishwasher.

Linen

- All linen must be disposed of as 'infected' linen and be placed into a red alginate (water soluble) bag before being placed into a white plastic bag.

Theatre Cases

- Inform theatre.
- Place patient at end of theatre list
- All staff in contact with the patient should be known to have immunity to VZV.
- In cases of shingles, the area affected must be covered by clothing or if lesions weeping covered with a dressing where possible.
- Patient should be taken straight into theatre.
- The patient should be recovered in theatre.

Visits to other departments

- Kept to a minimum.
- Need for isolation should never jeopardize clinical need.
- No waiting in communal areas.

Visitors

- Informed of risk by ward staff.
- Seek evidence of VZV immunity by verbal confirmation.

- To use PPE for patient contact if VZV immunity not known.
- If non-immune to discourage from visiting.

VZV Post-exposure prophylaxis

Varicella Zoster Immunoglobulin (VZIG)

Table 6. VZIG Dose to Be Given Per Age

Age	Dose
0-5 years	250mg
6-10 years	500mg
11-14 years	750mg
15+ years	1000mg
Given by slow intramuscular injection: the upper outer quadrant of the buttock or anterolateral thigh is the preferred location. Timing VZIG attenuates infection only if given within 10 days of contact.	

- If a second exposure occurs more than 3 weeks after a dose of VZIG, reassessment for a potential second dose is required as the protection offered is only temporary.
- Usage VZIG is generally indicated if VZV post-exposure prophylaxis is required for; neonates, and women in the first 20 weeks of pregnancy.

Acyclovir Dosage for prophylaxis

Table 7. Acyclovir Dosage for Prophylaxis

Age	Dose for prophylaxis
Children < 2 years-old	10 mg/kg four times daily
Children 2-17 years-old	10 mg/kg (to a maximum of 800mg) four times daily
Adults	800mg four times daily

- Oral acyclovir in the above doses should be given from days 7 to 14 after the exposure.
- For individuals identified more than 7 days post exposure, a course of acyclovir can be considered up to day 14 post exposure.
- If a second exposure to VZV occurs once the acyclovir course has been completed, reassessment should occur as a repeat course may be required.

- Contraindications For individuals with renal impairment or intestinal malabsorption, VZIG may be considered instead of acyclovir.

Neonates

- Neonates exposed to VZV should be discussed with virology to determine whether testing of the neonate or their mother is required to establish evidence of immunity.
- VZV post-exposure prophylaxis for neonates is with VZIG. Situations in which this is indicated include:
    - Neonates, whose mothers have developed chickenpox (not shingles) in the period 7 days before to 7 days after delivery.
    - Neonates 7 days old or less in contact with chickenpox or shingles whose mothers have no history of chickenpox and have no antibody.
    - VZV IgG negative infants in the first year of life, exposed to chickenpox or shingles whilst still undergoing prolonged or intensive special care nursing.
    - VZV IgG negative infants under 1 year old who have remained in hospital since birth and were born before 28 weeks gestation, or who weighed less than 1000g at birth.
- For very high-risk exposures, acyclovir may be required in addition to VZIG- discuss with virology.

Pregnant Women

- Immunocompetent pregnant women with a clear history of previous VZV infection (chickenpox or shingles) or immunization (two doses of varicella vaccine) should be considered immune, and no further action is required following a contact.
- Pregnant women without such a history should be tested for VZV IgG- on the booking blood if available.
- For pregnant women found to be VZV IgG not detected, post-exposure prophylaxis is indicated at all stages of pregnancy.
- If the exposure occurred in the first 20 weeks of pregnancy, prophylaxis with VZIG should be offered.
- For exposures occurring after 20 weeks of pregnancy, either VZIG or acyclovir can be used as prophylaxis, taking into account patient and health care professional preference, and the ability to provide prophylaxis in a timely fashion.

1.2.3 UK Health Security Agency Guidelines on Post Exposure Prophylaxis (PEP) for Varicella or Shingles (2023)

The UK Health Security Agency Guidelines has issued recommendations below[9]:

Post exposure prophylaxis is recommended for individuals who fulfil all the following 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

Types of post-exposure prophylaxis

1. **Antivirals (acyclovir or valaciclovir)**

- Oral acyclovir (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.
- Individuals in these groups who are exposed to chickenpox or shingles should be assessed and for those identified as susceptible antivirals (oral acyclovir 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 occasions 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 most reported side effects from acyclovir include dizziness, headache, nausea, vomiting, diarrhea, abdominal pain, skin rashes, photosensitivity, pruritus, urticaria and fatigue.
- In individuals with renal impairment or intestinal malabsorption, for example inflammatory bowel disease, VZIG may be considered. The dose of acyclovir 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.
- If VZIG is considered, it is important to demonstrate that the patient will benefit from the blood product by demonstrating that they are seronegative with VZV IgG antibody levels < 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 8. Recommended Doses of Oral Antivirals for PEP

	Oral Acyclovir	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 ofage	10mg/kg (up to a maximum of800mg), 4 times daily, from days 7 to 14 after exposure	20mg/kg (up to a maximum 1,000mg) 3 times daily, from days 7 to 14 after exposure
Adults	800mg 4 times daily, from days7 to 14 after exposure	1,000mg 3 times daily, from days 7 to 14 after exposure

- Although acyclovir and valaciclovir are not currently licensed for post-exposure prophylaxis for chickenpox, their use in the treatment of chickenpox is well established.
- Clinicians can prescribe medicines outside the terms of the license when it is in the best interest of the patient based on available evidence.
- 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.

Table 9. VZIG Dosage for Prophylaxis

Age	Dose
0 to 5 years	250mg
6 to 10 years	500mg
11 to 14 years	750mg
15 years and older	1,000mg

- 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 occasions.
- 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.
- Individuals receiving regular IVIG replacement therapy do not require VZIG if the most recent dose was administered <= 3 weeks before exposure.

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.

Pregnant women

- 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 light of the existing evidence on the safety of acyclovir, the efficacy of acyclovir 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 or shingles for susceptible women exposed in any stage of pregnancy.
- All pregnant women who are exposed to chickenpox or shingles should be assessed for susceptibility. If there is a previous history of chickenpox in the pregnant woman, she can be reassured, 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), acyclovir (800mg 4 times/day from days 7 to 14 after exposure) is recommended. Oral valaciclovir 1,000mg 3 times a daycan 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 occasions respectively. If the woman presents later than day 7 after exposure, a 7-day course of antiviralscan be started up to day 14 after exposure, if necessary.
- 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 acyclovir. Given the short half-life of acyclovir 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.
- If a pregnant woman presents with a chickenpox rash, they should be changed to a therapeutic dose (acyclovir 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 hospitalized and given IV acyclovir.

Infants and neonates

- 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 aqualitative assay or <150 mIU/ml by a quantitative assay.

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

1.2.4 Management of Herpesvirus Reactivations in Patients with Solid Tumors and Hematologic Malignancies: Update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) on Herpes Simplex Virus Type 1, Herpes Simplex Virus Type 2, and Varicella Zoster Virus (2022)

The AGIHO/DGHO Clinical Practice Guidelines[12] have opted for the following Grading Scheme/Level of Evidence:

Table 10. Grading the Certainty of Evidence and Strength of Recommendations of AGIHO/DGHO Clinical Practice Guidelines

Strength of recommendation (SoR)	**Definition**
A	Strongly supports a recommendation for use
B	Moderately supports a recommendation for use
C	Marginally supports a recommendation for use
D	Supports a recommendation against use
Quality of evidence (QoE)—level	**Definition**
I	Evidence from at least one properly designed randomized, controlled trial
II	Evidence from at least one well-designed clinical trial, without randomization; from cohort- or case-controlled analytic studies (preferably from > 1 center); from multiple time series; or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies, or reports of expert committees
Quality of evidence (QoE) – index, for level II	**Definition**

r	Meta-analysis or systematic review of randomized controlled trials
t	Transferred evidence, that is, results from different patient cohorts, or similar immune-statussituation
h	Comparator group is a historical control
u	Uncontrolled trial

The AGIHO/DGHO Clinical Practice Guidelines has issued recommendations below[12]:

- Acyclovir has long been the primary choice for prophylaxis and treatment of HSV (herpes simplex virus) and VZV (varicella-zoster virus) in immunocompromised patients.
- Recommendations include oral acyclovir 400 mg BID or 400 mg QID as prophylaxis for oral HSV disease (AIIr).
- Oral valacyclovir can be an alternative (BI), but the best regimen (250 mg BID or 500 mg BID) has not yet been defined.
- For patients not tolerating oral medication, intravenous acyclovir 250 mg/m2 TID is suitable (AIIr).
- Long-term (6 to 12 months) oral administration of acyclovir, valacyclovir, or famciclovir suppresses genital herpes in patients with frequent recurrences (suppressive therapy). Acyclovir 400 mg BID is widely used and tested (AI); valacyclovir 500 mg BID and famciclovir 500 mg BID are approved for this indication in immunocompromised patients (BIIt).
- Acyclovir has demonstrated efficacy in reducing clinical VZV reactivation and increasing survival in HSCT (hematopoietic stem cell transplant) recipients.
- Antiviral prophylaxis with acyclovir is standard of care in allogeneic and autologous HSCT recipients and non-HSCT patients undergoing tumor treatment. Recommendations include oral acyclovir to reduce clinical VZV reactivation, with dosages ranging from 400 mg once daily to 400 mg TID (AII).
- Valacyclovir may also be effective, but evidence is limited (CIIu).
- For patients not tolerating oral medication, intravenous acyclovir is suitable, but evidence on the most appropriate dosage is lacking (BIIt).
- It's essential to note that all three nucleoside analogues (acyclovir, valacyclovir, famciclovir) require dose adjustment in patients with renal impairment.

Vaccination

- Highly effective vaccines are available for VZV. The live-attenuated varicella virus (vOKA) was introduced during childhood for primary prophylaxis against VZV.
- Two types of herpes zoster vaccines, Zostavax® (live-attenuated, contraindicated in immunocompromised individuals) and Shingrix® (adjuvanted recombinant subunit), have been studied and approved, with Shingrix® being the preferred option for immunocompromised individuals.
- The recombinant zoster vaccine Shingrix® is recommended for the prevention of herpes zoster and post-herpetic neuralgia in adults aged 50 years or older and adults at an increased risk of herpes zoster.
- Despite the preliminary nature of data on clinical efficacy in certain malignancies and limited information on long-term protection rates, vaccination with Shingrix® is recommended due to its safety and immunogenicity. However, for specific high-risk patient groups, such as those with hematologic malignancies, it is suggested to consider additional acyclovir prophylaxis until more comprehensive data, especially from comparative trials between vaccination and pharmacological prophylaxis, become available.
- Increased adoption of Shingrix® in immunosuppressed patients, if clinically proven effective, is anticipated to reduce the reliance on pharmacological prophylaxis, pending further evidence.

Table 11. Recommendations for Pharmacological Prophylaxis in Patients with Solid Tumors

Clinical situation	Intention	Intervention	SoR	QoE	Comments
Patients with solid tumors and systemic therapy (in general; for specific risks see below) Patients with HNSCC, treated with radio chemotherapy	To prevent HSV/VZV reactivation	Acyclovir	D	III	Low risk of reactivation

Patients with HNSCC, treated with radio chemotherapy	To prevent HSV stomatitis	Acyclovir	C	IIr	
Patients with malignancies, taking corticosteroids in high doses long term (> 10 mg PEQ per day for 14 days or longer)	To prevent herpes zoster	Acyclovir	C	IIu	Persisting risk for several months after corticosteroid has been stopped

Table 12. Recommendations for Pharmacological Prophylaxis in Patients with Acute Leukemia and Myeloproliferative Neoplasms

Clinical situation	Intention	Intervention	SoR	QoE	Comments
Patients with AML/high-risk MDS, planned for intensive therapy	To prevent HSV stomatitis and other clinical manifestations of HSV To prevent herpes zoster (and other clinical reactivation of VZV)	Acyclovir, valacyclovir[a]	B	IIr	For remission induction chemotherapy
Patients with ALL	To prevent HSV stomatitis and other clinical manifestations of HSV	Acyclovir	B	I	Particularly in patients with APL treated with arsenic trioxide
	To prevent herpes zoster[b]	Acyclovir	B	III	While on treatment

Patients with MPN, treated with ruxolitinib	To reduce HSV disease	Acyclovir	C	IIu	
	To prevent herpes zoster[b]	Acyclovir	B	IIru	

[a] Valacyclovir may be used as well, although trials are limited compared to acyclovir.

[b] Data are mainly available for herpes zoster; evidence for other clinical reactivations of VZV is unclear.

Table 13. Patients with Lymphoma, Chronic Lymphocytic Leukemia, and Multiple Myeloma

Clinical situation	Intention	Intervention	SoR	QoE	Comments
Patients with non-Hodgkin lymphoma, treated with immune-chemotherapy[a]	To reduce HSV/VZV disease	Acyclovir (valacyclovir)[b]	B	IIu	Persisting risk for several months after therapy
	To reduce mortality	Acyclovir	C	IIah	Together with cotrimoxazol, in patients aged>60 years
Patients with Hodgkin's disease[a]	To prevent herpes zoster	Acyclovir (valacyclovir)[b]	C	III	
Patients with CLL receiving immuno-chemotherapy	To reduce HSV/VZV disease	Acyclovir (valacyclovir)[b]	B	IIuh	Persisting risk for several months after therapy (see text)
Patients with CLL (and other non-Hodgkin lymphoma) receiving BTK or BCL2 inhibitors[a]	To prevent herpes zoster (to reduce VZV/HSV disease)	Acyclovir (valacyclovir)[b]	C	IIu	Of benefit particularly in advanced lines of therapy
Patients with CLL (and other non-Hodgkin	To reduce HSV/VZV disease	Acyclovir	B	III	High general risk of opportunistic infections, persisting for

lymphoma) receiving idelalisib					several months after therapy
Patients with MM, receiving bortezomib	To reduce VZV disease[c]	Acyclovir, valacyclovir	A	IIu	[d]
Patient with MM receiving carfilzomib	To reduce VZV disease[c]	e.g., acyclovir	B	IIu	[d]
Patients with MM receiving ixazomib	To reduce VZV disease[c]	e.g., acyclovir	A	IIu	[d]
Patients with MM receiving lenalidomide	To reduce VZV disease[c]	e.g., acyclovir	A	IIh	[d]
Patients with MM receiving daratumumab	To reduce VZV disease[c]	e.g., acyclovir	C	IIh	[d]
Patients with MM receiving elotuzumab	To reduce VZV disease[c]	e.g., acyclovir	C	IIt	[d]
Patients with MM receiving conventional-dose chemotherapy[e] or other targeted agents[a]	To reduce VZV disease[c]	e.g., acyclovir	C	IIt	[d]

[a] Individual risk assessment is recommended: The following risk factors have been described in patients with non-Hodgkin lymphoma or CLL: age>60 years, concomitant treatment with high doses of corticosteroids (cumulative PEQ dose >2500 mg/m2 BSA), advanced line of therapy, type of therapy (bendamustine, maintenance by anti-CD20 monoclonal antibodies), history of febrile neutropenia, and history of HSV/VZV reactivation. The risk factors may also help in decision making for antiviral prophylaxis in patients with multiple myeloma.

[b] Valacyclovir has been used as well, but the evidence is less clear.

[c] VZV disease: data mainly refer to herpes zoster. Data on HSV disease is rarely reported.

[d] Reactivation risk by a single agent is difficult to determine because combinations were mainly used; prophylaxis in trials was frequently open ("might be considered or recommended"), and duration of prophylaxis has not been determined.

[e] Excluding patients with multiple myeloma treated with high-dose chemotherapy and autologous HSCT. For those antiviral pharmacological prophylaxis is highly recommended: A IIt (to prevent HSV reactivation) and A IIu (to prevent VZV reactivation).

Treatment

- The decision to initiate treatment is typically based on clinical diagnosis, often preceding or occurring without confirmation through virus detection.
- Treatment choices are influenced by factors such as (a) the type and severity of HSV or VZV reactivation, (b) the patient's clinical condition, and (c) the degree of immunosuppression.
- Oral administration is suitable for localized diseases with minor symptoms and mild immunosuppression. In such cases, alternatives to oral acyclovir (400 mg five times per day for localized HSV disease or 800 mg five times per day for herpes zoster) include valacyclovir (1000 mg three times per day) and famciclovir (500 mg twice or three times per day for herpes genitalis or herpes zoster).
- However, data are primarily derived from immunocompromised patients with HIV. The duration of therapy is typically 7 to 10 days.
- Close clinical monitoring is crucial during therapy, and a switch to intravenous acyclovir is recommended if signs of cutaneous dissemination, involvement of the central nervous system, or other organ complications emerge.
- For patients with severe immunosuppression and a high risk of complications, initial intravenous therapy is advisable, and early effective therapy is essential to minimize complication rates. Intravenous acyclovir is administered at 5 mg/kg body weight three times per day for localized HSV disease and 10 mg/kg body weight three times per day for disseminated, cerebral, or visceral disease of HSV and VZV, as well as for herpes zoster. The treatment duration for disseminated disease, cerebral, and visceral disease is at least 14 days.
- In general, treatment recommendations for patients with malignancies align with those for the general population, as specific trials for malignancy patients have not been conducted.
- It is important to note that brivudin is not approved for immunocompromised patients and is contraindicated, particularly in patients treated with 5-fluorouracil or its prodrugs (such as capecitabine, tegafur), due to potential lethal hematologic toxicity.

1.2.5 National Health Service Greater Glasgow and Clyde (NHSGGC) Pediatrics for Health Professionals Management of Varicella Zoster Infection (Chickenpox) in Children (2022)

The NHSGGC has issued recommendations below[10]:

High risk patient groups requiring admission

The subsequent individuals are susceptible to experiencing severe infection and necessitate hospitalization:

1. Infants aged less than one month
2. Immunocompromised children
3. Children exhibiting ongoing lesion development beyond day 5, posing a risk of disseminated disease
4. Children facing significant complications (bacterial secondary infection, neurological, or respiratory complications)

Antiviral treatment

- In immunocompetent children aged over 1 month and in good health, antiviral treatment is typically unnecessary.
- For at-risk children with the potential for moderate disease, consider oral Acyclovir for a duration of FIVE days.
- The following categories of children should be administered oral Acyclovir for FIVE days:
    - Those over 13 years old presenting within the initial 24 hours
    - Individuals with concurrent severe skin conditions like eczema
    - Children with underlying pulmonary diseases such as Cystic Fibrosis, chronic lung disease, asthma requiring inhaled steroids, or interstitial lung disease
    - Children taking aspirin
    - Those presently receiving short-course or intermittent oral corticosteroids (e.g., 1-2 mg/kg prednisolone) for viral-induced wheezing or asthma exacerbation
- It is crucial to counsel families on maintaining adequate fluid intake while the child is on acyclovir.
- For the following cases, initiate IV acyclovir following the BNF-c guidelines or refer to the West of Scotland Neonatal drug monographs for neonates:

- Babies under 1 month: 7 days of treatment

  Note: Well infants with a low number of lesions, and whose mothers have a history of chickenpox, may not require the full 7 days of treatment. Consultation with Infectious Disease specialists should be sought in such cases after 48 hours of treatment.

- Immunocompromised Children: 7 days of treatment or until no new lesions for 48 hours
- Children still developing new lesions for more than 5 days: Treat until 48 hours after the appearance of the last lesions.
- Children admitted with virally mediated complications or serious bacterial complications with ongoing new lesions.

- Consider IV acyclovir for severe varicella in children not previously identified as immunodeficient, as this could indicate severe immune compromise.
- It is important to note that Acyclovir is renally excreted and has been associated with renal impairment, especially in dehydrated patients. Adequate hydration should be maintained, and a low threshold for considering IV fluids is recommended. Accurate fluid balance should be recorded, and U&Es with creatinine should be monitored every 2-3 days or daily in patients with underlying renal dysfunction.

Symptomatic treatment for all Children

- Paracetamol for fever
- Topical calamine can be used but there is no evidence basis, and it can be felt to dry the skin and increase itching
- Antihistamines (e.g., chlorphenamine) can be used for itch
- Parents should be advised to keep children's nails short, cover affected skin with loose light clothing and encourage oral fluids
- **NSAIDS (e.g Ibuprofen) should be avoided.**

Post-exposure prophylaxis

- The goal of post-exposure prophylaxis is to safeguard individuals at high risk of severe chickenpox, testing negative for varicella IgG, and meeting the following criteria:
  - **Significant Exposure:** Individuals with substantial exposure to chickenpox or shingles during the infectious period.

        - **Risk-Increasing Condition:** Those with a medical condition that elevates the risk of severe chickenpox.
    - For a high-risk child of unknown antibody status exposed to chickenpox, urgent antibody status checking is necessary. If there's no known history of chickenpox, prophylaxis should be administered from day 7 to day 14 post-exposure*. In cases suggestive of previous varicella infection, prophylaxis should commence upon obtaining a negative antibody result (VZV IgG <150mIU/ml), with discussions involving the child's overall medical care team.
    - For patients presenting after day 7 of exposure, a 7-day antiviral course can begin as soon as possible and extend up to day 14 post-exposure if needed.

*The day of exposure is defined as the date of rash onset if the index case is a household contact OR the date of the first or only contact for exposure on multiple or single occasions, respectively.

- Patients receiving regular intravenous or subcutaneous immunoglobulin do not require additional prophylaxis. In cases of uncertainty regarding whether a child should receive post-exposure prophylaxis, contact their relevant medical team. Rheumatology has separate guidance and should be directly consulted for advice.
- Both Varicella immunoglobulin (VZIG) and oral acyclovir are suitable for prophylaxis. However, the UK Health Security Agency (formerly Public Health England) and Public Health Scotland now recommend that most patients (excluding neonates exposed within 7 days of delivery) should be managed with a high dose of oral acyclovir for 7 days, starting on day 7 post-exposure.
- In cases where a patient presents after day 7 of exposure, a 7-day course of antivirals can be initiated as soon as possible and continued up to day 14 post-exposure, if necessary.
- Patients may still contract chickenpox despite prophylactic treatment and should be advised to promptly seek medical attention if symptoms develop.
- In situations where concerns exist about malabsorption or oral antivirals are contraindicated, VZIG should be considered and administered as soon as possible within 7 days of exposure. For patients presenting after 7 days, there may still be a benefit in giving VZIG up to 10 days post-exposure. Varicella antibodies should be checked, and VZIG should only be given if negative or the result is <150mIU/ml.
- If a patient presents following a second exposure, they should be reassessed, and blood should be taken for varicella IgG. If they have not seroconverted, a further course of acyclovir is required (including patients who have just completed a course of antivirals), starting 7 days after the subsequent

exposure. Patients who have recently received VZIG and have a second exposure may need a further dose if the first dose was given more than 3 weeks ago. If the exposure was significant, a further dose should be given within 3-6 weeks following the initial administration of VZIG without further testing. If more than 6 weeks following VZIG, antibody levels should be rechecked, and a decision to treat should be made based on the results.

Post-exposure prophylaxis in neonates

- Infants at the highest risk of severe disease are those born to mothers who contract chickenpox (not shingles) within the period ranging from 7 days before to 7 days after delivery.
- For these infants, Intramuscular Varicella Zoster Immune Globulin (IM VZIG) should be administered as soon as possible, either within 7 days of birth or within 7 days of the onset of the disease in the mother if this occurs later. Additionally, for the highest-risk infants whose mothers develop varicella between 4 days before delivery and 48 hours post-delivery, there is a recommendation to consider admission for a 5-day course of intravenous acyclovir prophylaxis. This prophylaxis should commence on day 7 of maternal varicella.

Post-exposure prophylaxis is also advised for the following scenarios:

- Infants of non-immune mothers (Varicella IgG < 150 mIU/ml) who experience a significant non-maternal exposure within the first 7 days of life. In cases where the mother has no or uncertain history of chickenpox or has received the varicella vaccine, urgent antibody testing of the mother is recommended before treatment, if possible.
- Infants (under 1 year) who have remained in the hospital since birth and were born before 28 weeks of gestation or had a birth weight below 1 kg and are non-immune or have a varicella IgG level < 150mIU.
- Infants with severe congenital or underlying conditions necessitating prolonged intensive or special care during the first year of life and who are non-immune or have a varicella IgG level <150mIU/ml. In such cases, oral or intravenous acyclovir can be considered as an alternative to VZIG after exposure. If the infant is over 4 weeks old (regardless of gestation at birth), oral acyclovir is the preferred option unless contraindicated. Acyclovir initiation occurs on day 7 post-exposure. If contraindicated, VZIG should be administered.
- It is important to note that approximately 50% of infants given VZIG may still develop chickenpox, but the course is likely to be milder. Parents should be

instructed to bring the infant to the hospital if symptoms or signs of chickenpox develop. The incubation period of chickenpox in infants who have received VZIG can extend up to 28 days.

1.2.6 Molluscum Contagiosum: An Update and Review of New Perspectives in Etiology, Diagnosis, and Treatment (*Clinical, Cosmetic and Investigational Dermatology*, 2019)

Molluscum contagiosum (MC) is a self-limited infectious dermatosis, frequent in the pediatric population, sexually active adults, and immunocompromised individuals. It is transmitted mainly by direct contact with infected skin and clinically is characterized by umbilicated pink or skin-colored papules. The need for active treatment for MC is controversial; however, there is a consensus that it should be indicated in cases of extensive disease, associated with complications or aesthetic complaints. There are several treatment modalities which include mechanical, chemical, immunomodulatory, and antivirals. The objective of this article is to review the current evidence in etiology, clinical manifestations, diagnosis, and management alternatives of MC[13].

- Currently, the appropriateness of active treatment for patients with MC is a subject of controversy, given the self-limiting nature of the infection, the abundance of therapeutic options, and the absence of conclusive evidence defining optimal therapy.
- Consensus suggests that treatment is warranted in cases of extensive disease, secondary complications (such as bacterial superinfection, molluscum dermatitis, conjunctivitis), or aesthetic concerns.
- For all patients, general measures to prevent MCV spread are recommended. Patients should be advised against scratching or rubbing lesions, and sharing towels, tubs, or bath utensils should be avoided.
- Active treatments fall into categories such as mechanical, chemical, immunomodulatory, and antiviral methods.

Mechanical methods

- Cryotherapy, administered with a cotton-tipped swab or portable sprayers, has shown efficacy, with complete clearance rates ranging from 70.7% to 100% in various studies. However, drawbacks include the potential for blistering, scarring, and hypo or hyperpigmentation.
- Curettage, involving physical lesion removal, has proven effective, with one study reporting a complete clearance of 80.3% after a single session. Pain, bleeding, and scarring are potential side effects.

Chemical methods

- Cantharidin, an inhibitor of phosphodiesterase, induces an intraepidermal blister, resulting in variable cure rates (15.4% to 100%). Caution is advised in facial and anogenital regions due to the risk of bacterial superinfection.
- Potassium hydroxide, dissolving keratin, has shown clearance rates of 58.8% to 64.3%, comparable to other treatments.

Immunomodulatory methods

- Imiquimod, an immune-stimulatory agent, has demonstrated mixed efficacy in studies, with potential adverse effects including pain, blistering, scars, and pigmentary changes. Its current status as a therapeutic alternative is controversial.
- Other methods include oral cimetidine, interferon alfa, candidin, and diphencyprone.

Antivirals

- Cidofovir, an antiviral used in immunosuppressed patients, can be administered topically or intravenously, with the latter posing nephrotoxicity risks.

1.2.7 Guidelines for the Treatment of Measles by Centers for Disease Control and Prevention (CDC) of America (November 5, 2020)

The CDC has issued recommendations below[14]:

- Treatment for measles does not involve specific antiviral therapy. Instead, medical care is supportive, aiming to alleviate symptoms and manage complications, especially bacterial infections.
- In cases of severe measles in children, particularly those requiring hospitalization, vitamin A treatment is recommended. Immediate administration upon diagnosis and a repeat dose the following day are advised. The recommended daily doses vary based on age:
    - 50,000 IU for infants below 6 months;
    - 100,000 IU for infants aged 6–11 months;
    - 200,000 IU for children aged 12 months and older.

Vaccine Recommendations

Children

- The CDC recommends routine childhood immunization with the MMR vaccine, starting with the first dose between 12 and 15 months of age, and the second dose at 4 through 6 years or at least 28 days after the first dose. The MMRV vaccine is also available for children aged 12 months through 12 years, with a minimum interval of three months between doses.

Students at Post-High School Educational Institutions

- Students without evidence of measles immunity at post-high school educational institutions should receive two doses of the MMR vaccine. The second dose should be administered no earlier than 28 days after the first dose.

Adults

- Individuals born in 1957 or later without evidence of measles immunity should receive at least one dose of the MMR vaccine.

International Travelers

- People aged 6 months or older traveling internationally should be protected against measles. Recommendations include:
    - Infants aged 6-11 months: one dose of MMR vaccine
    - Children aged 12 months or older: documentation of two doses of MMR vaccine, with the first dose administered at 12 months or older and the second at least 28 days later.
    - Teenagers and adults born in 1957 or later: documentation of two doses of MMR vaccine, with the second dose administered at least 28 days after the first.

*Note: Infants receiving one dose of MMR vaccine before their first birthday should follow the recommended schedule for two additional doses (at 12-15 months and 4-6 years or at least 28 days later).

*Additionally, the MMRV vaccine is available for children aged 12 months through 12 years, with the first dose administered at 12 months or older and the second dose at least three months later. MMRV is not recommended for those older than 12 years of age.

Post-exposure prophylaxis

- Post-exposure prophylaxis (PEP) is recommended for individuals exposed to measles who cannot promptly demonstrate immunity.
- To potentially offer protection or alter the disease's clinical course in susceptible individuals, MMR vaccine should be administered within 72 hours of initial measles exposure, or immunoglobulin (IG) within six days of exposure. It is crucial to avoid simultaneous administration of MMR vaccine and IG, as this practice renders the vaccine ineffective.

Isolation

- Isolation measures for individuals infected with measles involve maintaining isolation for a period of four days after the onset of a rash. In healthcare settings, airborne precautions should be strictly followed.
- Due to the slight possibility of MMR vaccine failure in healthcare providers exposed to infected patients, all healthcare personnel caring for individuals with measles should adhere to airborne precautions.
- The recommended placement for patients requiring airborne precautions is in a single-patient airborne infection isolation room (AIIR).
- Regardless of presumptive immunity status, all healthcare staff entering the room should use respiratory protection consistent with airborne infection control precautions, such as an N95 respirator or a respirator with similar effectiveness in preventing airborne transmission.

Section 2.0 Drug Therapy in Viral Skin Infections

This section comprises four subsections: the first contains the newly recommended drugs, the second covers drug modifications, the third outlines the drugs to delist due to withdrawal from the market among others, and the fourth tackles other drugs approved by FDA/EMA but not yet SFDA-registered.

2.1 Additions

No new drugs have been approved by the SFDA for the treatment of Viral Skin Infections since April 2020.

2.2 Modifications

The following modifications and adjustments have been implemented since the 2020 report:

Table 14. PE Modifications for Drugs Treating Viral Skin Infections

Drugs	PE modifications
FAMCICLOVIR for chickenpox (varicella)	Add ST: famciclovir is generally not the first-line treatment for uncomplicated chickenpox, especially in healthy individuals. the preferred antiviral medications for chickenpox are acyclovir and valacyclovir
FAMCICLOVIR for herpes simplex virus (herpes labialis)	Add ST: famciclovir is not typically considered a first-line treatment for herpes labialis (cold sores) caused by the herpes simplex virus (HSV). first-line treatments usually include medications like acyclovir and valacyclovir.
FAMCICLOVIR for herpes zoster (shingles)	Add ST: famciclovir is generally not the first-line treatment for zoster.
PODOPHYLLOTOXIN	Add AGE: not to be used in children <12 years of age
VARICELLA ZOSTER VIRUS GLYCOPROTEIN E ADJUVANTED WITH AS01B	Add AGE: zoster vaccine is not a substitute for varicella vaccine and should not be used in children and adolescents.

2.3 Delisting

No medications have been withdrawn or are no longer recommended for the treatment of viral skin infections since April 2020.

2.4 Other Drugs

The drug detailed in this section is a topical solution used for Molluscum Contagiosum recently **approved** by the FDA but **not registered by the SFDA**.

Cantharidin

Cantharidin was approved by the FDA on July 24, 2023. It is indicated for the topical treatment of molluscum contagiosum in adult and pediatric patients 2 years of age and older. Cantharidin works by causing blistering at the site of application, and this blistering can help remove the molluscum bumps. It is for topical use only. Not for oral, mucosal, or ophthalmic use. It should be applied a single application directly to each lesion every 3 weeks as needed, and the patient should remove it with soap and water 24 hours after treatment[15].

Section 3.0 Key Recommendations Synthesis

Managing People at High Risk for Severe Varicella

Varicella-Zoster Immune Globulin

- Recommend varicella-zoster immune globulin for individuals unable to receive the varicella vaccine, particularly those lacking evidence of immunity, facing probable infection due to exposure, or at high risk for severe varicella.
- Administer promptly after exposure to VZV preferably within 10 days of exposure [7].

Acyclovir Treatment

- Recommend oral acyclovir or valacyclovir treatment for high-risk groups, including healthy individuals above 12 years old, those with chronic cutaneous or pulmonary disorders, and individuals receiving certain therapies.
- Administer oral therapy within 24 hours after the onset of varicella rash for maximum effectiveness.
- Intravenous acyclovir is advised for pregnant women with varicella, especially in the second and third trimesters, and for severe cases (disseminated VZV, pneumonia, encephalitis, thrombocytopenia, severe hepatitis).
- Famciclovir is not established for children; use Foscarnet for acyclovir-resistant VZV strains, consulting an infectious disease specialist[7].

Assessing Immunity to Varicella

- Administer two doses of varicella vaccine for all individuals without evidence of immunity.
- Individuals with no epidemiologic link or laboratory confirmation of varicella should receive a second vaccine dose[7].

Chickenpox treatment

- Administration of Varicella Zoster Immunoglobulin (VZIG) can prolong incubation period to 28 days.
- There is no role for VZIG in the management of acute cases of chickenpox.
- Use of high dose acyclovir should be considered early in infection for adults and immunocompromised patients[8].

Shingles treatment

- If required is with either oral or intravenous acyclovir depending on disease severity and underlying health conditions[8].

VZV 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[9].

Types of VZV PEP:

Oral acyclovir

- Oral acyclovir (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.
- Individuals in these groups who are exposed to chickenpox or shingles should be assessed and for those identified as susceptible antivirals (oral acyclovir or valaciclovir) should be given from day 7 to day 14 after exposure[9].

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.
- VZIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts) of the day of exposure[9].

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)[9].

VZV in pregnant women

- Immunocompetent pregnant women with a confirmed history of previous varicella-zoster virus (VZV) infection or immunization are considered immune, requiring no further action following exposure.

- Pregnant women without such a history should undergo testing for VZV IgG during booking blood, and if the result is negative, post-exposure prophylaxis is recommended throughout pregnancy.
- If exposure occurs in the first 20 weeks, VZIG prophylaxis is advised, while exposures after 20 weeks allow for a choice between VZIG and acyclovir, considering patient and healthcare professional preferences and the ability to administer timely prophylaxis (VZIG offered if the woman is unable to take oral antivirals due to malabsorption or renal toxicity)[8].

VZV in neonates

VZV post-exposure prophylaxis for neonates is with VZIG. Situations in which this is indicated include:

- Neonates, whose mothers have developed chickenpox (not shingles) in the period 7 days before to 7 days after delivery.
- Neonates 7 days old or less in contact with chickenpox or shingles whose mothers have no history of chickenpox and have no antibody.
- VZV IgG negative infants in the first year of life, exposed to chickenpox or shingles whilst still undergoing prolonged or intensive special care nursing.
- VZV IgG negative infants under 1 year old who have remained in hospital since birth and were born before 28 weeks gestation, or who weighed less than 1000g at birth.

For very high-risk exposures, acyclovir may be required in addition to VZIG- discuss with virology[8, 10].

VZV in children

- In immunocompetent children aged over 1 month and in good health, antiviral treatment is typically unnecessary.
- For at-risk children with the potential for moderate disease, consider oral Acyclovir for a duration of FIVE days.
- Consider IV acyclovir for severe varicella in children not previously identified as immunodeficient, as this could indicate severe immune compromise[10].

VZV in children symptomatic treatment

- Paracetamol for fever
- Topical calamine can be used but there is no evidence basis, and it can be felt to dry the skin and increase itching
- Antihistamines (e.g. chlorphenamine) can be used for itch
- NSAIDS (e.g. Ibuprofen) should be avoided[10].

PEP in children

- Both Varicella immunoglobulin (VZIG) and oral acyclovir are suitable for prophylaxis
- If there's no known history of chickenpox, prophylaxis should be administered from day 7 to day 14 post-exposure
- For patients presenting after day 7 of exposure, a 7-day antiviral course can begin as soon as possible and extend up to day 14 post-exposure if needed
- In situations where concerns exist about malabsorption or oral antivirals are contraindicated, VZIG should be considered and administered as soon as possible within 7 days of exposure. For patients presenting after 7 days, there may still be a benefit in giving VZIG up to 10 days post-exposure. Varicella antibodies should be checked, and VZIG should only be given if negative or the result is <150mIU/ml[16].

Management of Patients with Varicella-Zoster Infection:

- Patients with VZV infection must be isolated immediately in single rooms with closed doors and with no contact with persons without evidence of immunity, this must include visitors and healthcare workers.
- Respiratory precautions (chickenpox) and contact precautions (shingles) must be adhered to until all lesions are dry and crusted.
- The patient should be isolated until all the skin lesions are crusted which is usually about four to seven days after the appearance of the rash[8].

Management of Healthcare Personnel with Herpes Zoster

- For localized herpes zoster in an immunocompetent person
    - Cover lesions and restrict from care of high-risk patients (i.e., patients who are susceptible to varicella and at increased risk for complications of varicella, including neonates, pregnant women, and immunocompromised persons of any age) until all lesions are dry and scabbed.
    - If lesions cannot be completely covered, exclude from duty until all lesions are dry and scabbed[8].

Management of Healthcare Personnel Exposed to Someone with Herpes Zoster (one or more documented doses of the varicella vaccine or proof of varicella immunity):

- Do not require post-exposure prophylaxis and face no work restrictions.
- Ensure up-to-date immunization with two documented doses of the varicella vaccine.

- If only one documented dose has been received, the second dose should be administered within 3 to 5 days after exposure, provided at least 4 weeks have passed since the first dose[11].

Management of Healthcare Personnel Exposed to Someone with Herpes Zoster (without documented vaccination or evidence of varicella immunity):

- Should be furloughed or temporarily reassigned to locations distant from patient-care areas during this period.
- Should receive post-exposure vaccination:
  - recommended within 3 to 5 days of exposure to the rash. It remains effective even if administered 6 or more days after exposure, providing protection against subsequent exposures if the current exposure did not result in infection.
- Varicella zoster immune globulin is advised if at risk for severe disease and varicella vaccination is contraindicated, such as in pregnant healthcare personnel[11].

HSV/VZV prophylaxis for immunocompromised:

- Acyclovir has long been the primary choice for prophylaxis and treatment of HSV (herpes simplex virus) and VZV (varicella-zoster virus) in immunocompromised patients.
- Recommendations include oral acyclovir 400 mg BID or 400 mg QID as prophylaxis for oral HSV disease.
- Oral valacyclovir can be an alternative, but the best regimen (250 mg BID or 500 mg BID) has not yet been defined.
- For patients not tolerating oral medication, intravenous acyclovir 250 mg/m2 TID is suitable[12].

HSV/VZV prophylaxis for immunocompromised:

Long-term (6 to 12 months) oral administration of acyclovir, valacyclovir, or famciclovir suppresses genital herpes in patients with frequent recurrences (suppressive therapy). Acyclovir 400 mg BID is widely used and tested; valacyclovir 500 mg BID and famciclovir 500 mg BID are approved for this indication in immunocompromised patients[12].

HSV/VZV prophylaxis for immunocompromised:

Antiviral prophylaxis with acyclovir is standard of care in allogeneic and autologous HSCT recipients and non-HSCT patients undergoing tumor treatment. Recommendations include oral acyclovir to reduce clinical VZV reactivation, with dosages ranging from 400 mg once daily to 400 mg TID[12].

Vaccination in immunocompromised individuals:

Highly effective vaccines, including the live-attenuated varicella virus (vOKA) for primary prophylaxis against varicella-zoster virus (VZV), are available. Two herpes zoster vaccines, Zostavax® and Shingrix®, have been approved, with Shingrix® preferred for immunocompromised individuals. Shingrix® is recommended for adults aged 50 or older and those at increased risk of herpes zoster, despite limited long-term data. For high-risk groups like those with hematologic malignancies, considering additional acyclovir prophylaxis is suggested until more comprehensive data, especially from comparative trials, become available[12].

The decision to initiate treatment for (HSV) or (VZV) reactivation is based on clinical diagnosis, preceding confirmation through virus detection. Oral administration is suitable for localized diseases with minor symptoms and mild immunosuppression, with acyclovir, valacyclovir, and famciclovir. Duration of therapy: 7 to 10 days, with close clinical monitoring.

Intravenous acyclovir is recommended for severe cases, especially for patients with high immunosuppression and a risk of complications. Treatment duration for disseminated, cerebral, or visceral disease is at least 14 days. Treatment recommendations for patients with malignancies generally align with those for the general population[12].

Molluscum Contagiosum (MC) Treatment:

- Consensus recommends treatment for extensive disease, secondary complications (bacterial superinfection, molluscum dermatitis, conjunctivitis), or aesthetic concerns. General preventive measures for all patients include avoiding scratching, rubbing lesions, and sharing personal items.
- Active treatments are categorized into mechanical, chemical, immunomodulatory, and antiviral methods. Mechanical methods such as cryotherapy and curettage show efficacy, but drawbacks include potential blistering, scarring, and pigmentation changes. Chemical methods like cantharidin and potassium hydroxide exhibit variable cure rates, with caution in specific regions due to infection risks. Immunomodulatory methods, including imiquimod, oral cimetidine, interferon alfa, candidin, and diphencyprone, present mixed efficacy and controversies. Antivirals like cidofovir, used in immunosuppressed patients, can be administered topically or intravenously, with the latter carrying nephrotoxicity risks[13].

Measles treatment:

- Measles treatment does not involve specific antiviral therapy but focuses on supportive medical care to alleviate symptoms and manage complications, especially bacterial infections[14].

- Severe cases in hospitalized children may require vitamin A treatment, with recommended daily doses based on age[14].

Measles post-exposure Prophylaxis:

- PEP is recommended for those exposed to measles without prompt immunity demonstration. MMR vaccine or immunoglobulin (IG) should be administered within specified time frames to potentially offer protection[14].

Isolation:

- Infected individuals should be isolated for four days after the rash onset, with strict airborne precautions in healthcare settings[14].
- Healthcare providers caring for measles patients should observe airborne precautions, with preferred placement in a single-patient airborne infection isolation room (AIIR)[14].

Regardless of immunity status, healthcare staff should use respiratory protection like an N95 respirator when entering the room to prevent airborne transmission[14].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Viral Skin Infections report** and aims to provide recommendations to aid in the management of Viral Skin Infections. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Viral Skin Infections. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

Some covered drugs may have additional requirements, rules or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

Appendix B. Viral Skin Infections Scope

Section	Rationale/Updates
Section 1.3: CDC Chickenpox (Varicella) Treatment Guidelines **(2022)**[7]	**People at High Risk for Severe Varicella:** o Immunocompromised individuals lacking proof of immunity to varicella, such as: - Individuals diagnosed with leukemia or lymphoma - Individuals using immune system-suppressing medications like high-dose systemic steroids or chemotherapeutic agents - Individuals with cellular immune deficiencies or other issues with their immune system o Newborns born to mothers with varicella within five days before to two days after delivery. o Premature infants exposed to varicella or herpes zoster, specifically: - Hospitalized premature infants born at 28 weeks of gestation or later, with mothers lacking evidence of immunity - Hospitalized premature infants born at less than 28 weeks of gestation or weighing ≤1,000 grams at birth, regardless of their mothers' varicella immunity status. o Pregnant women lacking evidence of immunity to varicella. **Managing People at High Risk for Severe Varicella** **Recommendations for Varicella-Zoster Immune Globulin:** o For individuals exposed to varicella or herpes zoster unable to receive the varicella vaccine, consider varicella-zoster immune globulin (VariZIG™) to prevent the development or reduce the severity of varicella. This is particularly advisable for those who: - Lack evidence of immunity to varicella. - Face a probable infection due to exposure. - Are at high risk for severe varicella. o Administer VariZIG™ promptly after exposure to varicella-zoster virus (VZV), preferably within 10 days of exposure. **Recommendations for Acyclovir Treatment:**

	○ Consider oral acyclovir or valacyclovir treatment for the following high-risk groups at increased risk for moderate to severe varicella: - Healthy individuals above 12 years old. - Individuals with chronic cutaneous or pulmonary disorders. - Those receiving long-term salicylate therapy. - Individuals receiving short, intermittent, or aerosolized courses of corticosteroids. ○ Healthcare providers may opt for oral acyclovir or valacyclovir for secondary cases within a household. Administer oral therapy within the first 24 hours after the onset of the varicella rash for maximum effectiveness. However, AAP does not recommend oral acyclovir or valacyclovir for otherwise healthy children experiencing typical varicella without complications. ○ For pregnant women with varicella, especially in the second and third trimesters, some experts recommend oral acyclovir or valacyclovir. Intravenous acyclovir is advised for pregnant patients with serious viral-mediated complications, such as pneumonia. ○ Intravenous acyclovir therapy is recommended for severe disease (e.g., disseminated VZV, pneumonia, encephalitis, thrombocytopenia, severe hepatitis) and for varicella in immunocompromised patients (including those on high-dose corticosteroid therapy for >14 days). ○ While Famciclovir is available for treating VZV infections in adults, its efficacy and safety have not been established for children. In cases of infections caused by acyclovir-resistant VZV strains, typically occurring in immunocompromised individuals, Foscarnet should be used, with consultation from an infectious disease specialist recommended. **Assessing immunity to Varicella:** ○ Two doses of varicella vaccine are recommended for all children, adolescents, and adults without evidence of immunity to varicella. Those who previously received one dose of varicella vaccine should receive their second dose for best protection against the disease. ○ People who have neither an epidemiologic link nor laboratory confirmation of varicella should not be considered as having a valid history of disease. For these people, a second dose of vaccine is recommended if they previously received only one dose. If a healthcare

<table>
<tr><td></td><td>provider verifies the diagnosis based on the above criteria, then vaccination is not needed.</td></tr>
<tr><td>Addition of a new section:
CDC; Preventing Varicella-Zoster Virus (VZV) Transmission from Herpes Zoster in Healthcare Settings (2023)[11]</td><td>
Preventing Varicella in Healthcare Settings; Nosocomial Transmission of VZV

Nosocomial transmission of VZV is well-recognized and can be life threatening to certain groups of patients.
Patients, healthcare providers, and visitors with varicella or herpes zoster can spread VZV to susceptible patients and healthcare providers in hospitals, long-term-care facilities, and other healthcare settings. In healthcare settings, transmissions have been attributed to delays in the diagnosis or reporting of varicella and herpes zoster and failures to implement control measures promptly.

Management of Patients with Herpes Zoster

The approach to infection control is contingent upon the patient's immune status (immunocompetent or immunocompromised) and the extent of the rash, whether it is confined or disseminated (lesions present beyond the primary or neighboring dermatomes).
Irrespective of these factors, adhere to standard infection control measures. Refer to the table below to ascertain if supplementary infection control precautions are necessary.

<table>
<tr><th>Patient Immune Status</th><th>Localized Herpes Zoster</th><th>Disseminated Herpes Zoster</th></tr>
<tr><td>Immunocompetent</td><td>Completely cover lesions and follow standard precautions until lesions are dry and scabbed.</td><td>Airborne and contact precautions until lesions are dry and scabbed.</td></tr>
<tr><td>Immunocompromised</td><td>Airborne and contact precautions until disseminated infection is ruled out.
After dissemination is ruled out, completely cover lesions and follow standard precautions until lesions are dry and scabbed.</td><td>Airborne and contact precautions until lesions are dry and scabbed.</td></tr>
</table>
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	Management of Healthcare Personnel with Herpes Zoster o For localized herpes zoster in an immunocompetent person - Cover lesions and restrict from care of high-risk patients (i.e., patients who are susceptible to varicella and at increased risk for complications of varicella, including neonates, pregnant women, and immunocompromised persons of any age) until all lesions are dry and scabbed. - If lesions cannot be completely covered, exclude from duty until all lesions are dry and scabbed. o For disseminated herpes zoster or localized herpes zoster in an immunocompromised person until disseminated infection is ruled out: exclude from duty until all lesions are dry and scabbed. **Management of Healthcare Personnel Exposed to Someone with Herpes Zoster** **3. Healthcare personnel with one or more documented doses of the varicella vaccine or proof of varicella immunity:** o Do not require post-exposure prophylaxis and face no work restrictions. o Ensure up-to-date immunization with two documented doses of the varicella vaccine. • If only one documented dose has been received, the second dose should be administered within 3 to 5 days after exposure, provided at least 4 weeks have passed since the first dose. o **Practice self-monitoring or have the employee health program or an infection control nurse monitor** from the 8th day after the initial exposure through the 21st day after the last exposure. **Promptly report any symptoms such as fever, headache, skin lesions, or systemic issues.** • If symptoms manifest, healthcare personnel should be promptly removed from patient care, placed on sick leave, and provided with antiviral medication. **4. Healthcare personnel without documented vaccination or evidence of varicella immunity:** o Are considered susceptible to varicella-zoster virus (VZV) infection. o **May be potentially infectious** from the 8th day after the first exposure through the 21st day

	after the last exposure. ○ **Should be furloughed or temporarily reassigned** to locations distant from patient-care areas during this period. ○ **Should receive post-exposure vaccination** following guidelines from the Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC). • Vaccination is recommended within 3 to 5 days of exposure to the rash. It remains effective even if administered 6 or more days after exposure, providing protection against subsequent exposures if the current exposure did not result in infection. ○ **Varicella zoster immune globulin** is advised if at risk for severe disease and varicella vaccination is contraindicated, such as in pregnant healthcare personnel. • If varicella zoster immune globulin is used as post-exposure prophylaxis, the individual should be excluded from work from the 8th day after the first exposure through the 28th day after the last exposure. **Recommendations for healthcare institutions to prevent varicella and nosocomial spread** ○ Have documented evidence of varicella immunity for all healthcare personnel readily available at the healthcare personnel's work location. ○ Alert healthcare personnel without evidence of immunity to varicella about the risks of possible infection and offer those without evidence of immunity two doses of varicella vaccine, administered 4 to 8 weeks apart, when they begin employment. ○ Establish protocols and recommendations for screening and vaccinating healthcare personnel and for managing healthcare personnel after exposures in the workplace.
Addition of a new section: NHS; Clinical Guideline for the Management of Varicella-Zoster (VZV) Infections	**Chickenpox Treatment** ○ Incubation period is generally between 10 - 21 days, but usually 14 days. Administration of Varicella Zoster Immunoglobulin (VZIG) can prolong incubation period to 28 days. ○ There is no role for VZIG in the management of acute cases of chickenpox. ○ Use of high dose acyclovir should be considered early in infection for adults and immunocompromised patients. **Isolation**

to prevent nosocomial Transmission to at-risk individuals **(2023)**[8]	○ Person to person transmission occurs by direct contact, droplet and airborne spread of secretions from the respiratory tract or vesicles. The virus can be spread indirectly on hands and inanimate objects. ○ Respiratory isolation procedures are required i.e. single room with use of gloves, aprons, masks and attention to hand hygiene to prevent infection of non-immune staff and susceptible patients. ○ Patients with chickenpox should be cared for by immune staff only. **Shingles** ○ Shingles is less contagious (there is no infectious incubation period) as the virus is confined to a rash which can be covered in most cases. Non immune patients are at risk of contracting chickenpox from patients with shingles ○ Those who have had chickenpox who come into contact with a person with shingles are not at risk of acquiring the disease as they will be immune. **Isolation** ○ Person to person transmission is via direct contact with the rash or from spread of secretions from the rash to non-immune persons. ○ Contact isolation procedures are required i.e. single room with use of gloves and apron and attention to hand hygiene to prevent infection of non-immune staff and transfer of virus to susceptible patients. **Treatment** ○ If required is with either oral or intravenous acyclovir depending on disease severity and underlying health conditions. **Management of Patients with Varicella-Zoster Infection** ○ In the event of an infection with VZV occurring in hospital the following actions must be taken: Patients with VZV infection must be isolated immediately in single rooms with closed doors and with no contact with persons without evidence of immunity, this must include visitors and healthcare workers ○ Suspicion of VZV infection should be confirmed by sending a green viral swab of a lesion(s) for PCR.

	○ Respiratory precautions (chickenpox) and contact precautions (shingles) must be adhered to until all lesions are dry and crusted ○ The patient must be nursed in a side room with designated toilet facilities ○ Respiratory (chickenpox) and contact (shingles) precautions posters applied ○ Patients do not need to be nursed in negative pressure rooms ○ The patient should be isolated until all the skin lesions are crusted which is usually about four to seven days after the appearance of the rash ○ Offer patient chickenpox/shingles information leaflet ○ Non immune patients who have been exposed to the patient with Varicella Zoster infection and who are still in hospital should be isolated from 7 days following their first exposure until 21 days after their last exposure. This period is extended by 7 days if post-exposure prophylaxis is given because this can prolong the incubation period. **Personnel Protective Equipment (PPE)** ○ During the period of isolation, appropriate PPE must be worn for direct patient contact reflecting respiratory or contact precautions as required. ○ Hands must be decontaminated after the removal of gloves. Strict compliance with hand washing techniques must be observed at all times. ○ Eye protection should be considered dependent on the care activity being performed. Disposal of clinical waste ○ All waste from the room should be disposed of as clinical waste for the duration that the patient is in isolation. **Cutlery/Crockery** ○ Normal ward issue can be used but must be cleaned by washing in a dishwasher **Linen** ○ All linen must be disposed of as 'infected' linen and be placed into a red alginate (water soluble) bag before being placed into a white plastic bag **Theatre Cases** ○ Inform theatre ○ Place patient at end of theatre list

- All staff in contact with the patient should be known to have immunity to VZV
- In cases of shingles, area affected must be covered by clothing or if lesions weeping covered with a dressing where possible.
- Patient should be taken straight into theatre
- The patient should be recovered in theatre

Visits to other departments

- Kept to a minimum
- Need for isolation should never jeopardize clinical need
- No waiting in communal areas

Visitors

- Informed of risk by ward staff
- Seek evidence of VZV immunity by verbal confirmation
- To use PPE for patient contact if VZV immunity not known
- If non-immune to discourage from visiting

VZV Post-exposure prophylaxis

Varicella Zoster Immunoglobulin (VZIG)

Age	Dose
0-5 years	250mg
6-10 years	500mg
11-14 years	750mg
15+ years	1000mg
Given by slow intramuscular injection: The upper outer quadrant of the buttock or anterolateral thigh is the preferred location Timing VZIG attenuates infection only if given within 10 days of contact.	

- If a second exposure occurs more than 3 weeks after a dose of VZIG, reassessment for a potential second dose is required as the protection offered is only temporary.
- Usage VZIG is generally indicated if VZV post-exposure prophylaxis is required for; neonates, and women in the first 20 weeks of pregnancy.

Acyclovir Dosage for prophylaxis

Age	Dose for prophylaxis
Children < 2 years-old	10 mg/kg four times daily
Children 2-17 years-old	10 mg/kg (to a maximum of 800mg) four times daily
Adults	800mg four times daily

- Oral acyclovir in the above doses should be given from days 7 to 14 after the exposure.
- For individuals identified more than 7 days post exposure, a course of acyclovir can be considered up to day 14 post exposure.
- If a second exposure to VZV occurs once the acyclovir course has been completed, reassessment should occur as a repeat course may be required.
- Contraindications For individuals with renal impairment or intestinal malabsorption, VZIG may be considered instead of acyclovir.

Neonates

- Neonates exposed to VZV should be discussed with virology to determine whether testing of the neonate or their mother is required to establish evidence of immunity
- VZV post-exposure prophylaxis for neonates is with VZIG. Situations in which this is indicated include;
  - Neonates, whose mothers have developed chickenpox (not shingles) in the period 7 days before to 7 days after delivery.
  - Neonates 7 days old or less in contact with chickenpox or shingles whose mothers have no history of chickenpox and have no antibody.
  - VZV IgG negative infants in the first year of life, exposed to chickenpox or shingles whilst still undergoing prolonged or intensive special care nursing.
  - VZV IgG negative infants under 1 year old who have remained in hospital since birth and were born before 28 weeks gestation, or who weighed less than 1000g at birth.
- For very high risk exposures, acyclovir may be required in addition to VZIG- discuss with virology

	Pregnant Women o Immunocompetent pregnant women with a clear history of previous VZV infection (chickenpox or shingles) or immunization (two doses of varicella vaccine) should be considered immune and no further action is required following a contact. o Pregnant women without such a history should be tested for VZV IgG- on the booking blood if available. o For pregnant women found to be VZV IgG not detected, post-exposure prophylaxis is indicated at all stages of pregnancy. o If the exposure occurred in the first 20 weeks of pregnancy, prophylaxis with VZIG should be offered. o For exposures occurring after 20 weeks of pregnancy, either VZIG or acyclovir can be used as prophylaxis, taking into account patient and health care professional preference, and the ability to provide prophylaxis in a timely fashion.
Addition of a new section: UK Health Security Agency; Guidelines on post exposure prophylaxis (PEP) for varicella or shingles **(2023)**[9]	Post exposure prophylaxis is recommended for individuals who fulfil all of the following 3 criteria: o significant exposure to chickenpox (varicella) or shingles (zoster) during the infectious period o at increased risk of severe chickenpox such as immunosuppressed individuals, neonates and pregnant women o no antibodies to varicella-zoster virus (VZV) – urgent VZV antibody testing can be performed within 24 hours **Types of post-exposure prophylaxis** **4. Antivirals (acyclovir or valaciclovir)** o Oral acyclovir (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. o Individuals in these groups who are exposed to chickenpox or shingles should be assessed and for those identified as susceptible antivirals (oral acyclovir or valaciclovir) should be given from day 7 to day 14 after exposure. o 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 occasions 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 most commonly reported side effects from acyclovir include dizziness, headache, nausea, vomiting, diarrhea, abdominal pain, skin rashes, photosensitivity, pruritus, urticaria and fatigue.
- In individuals with renal impairment or intestinal malabsorption, for example inflammatory bowel disease, VZIG may be considered. The dose of acyclovir 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
- 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 < 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.

	Oral Acyclovir	Oral Valaciclovir
Infants over 4 weeks to children under 2 years age	10mg/kg 4 times daily, days 7to 14 after exposure	Not recommended
Children 2 to 17 years ofage	10mg/kg (up to a maximum of800mg), 4 times daily, from days 7 to 14 after exposure	20mg/kg (up to a maximum 1,000mg) 3 times daily, from days 7 to 14 after exposure
Adults	800mg 4 times daily, from days7 to 14 after exposure	1,000mg 3 times daily, fromdays 7 to 14 after

		exposure

- Although acyclovir 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 license when it is in the best interest of the patient on the basis of available evidence.
- 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.

5. 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.

Age	Dose
0 to 5 years	250mg
6 to 10 years	500mg
11 to 14 years	750mg
15 years and older	1,000mg

- 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 occasions.
- 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.
- Individuals receiving regular IVIG replacement therapy do not require VZIG if the most

	recent dose was administered <= 3 weeks before exposure. **6. Intravenous immunoglobulin (IVIG)** o 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. o 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. **Pregnant woman:** o 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. o 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. o In light of the existing evidence on the safety of acyclovir, the efficacy of acyclovir 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 or shingles for susceptible women exposed in any stage of pregnancy. o All pregnant women who are exposed to chickenpox or shingles should be assessed for susceptibility. 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), acyclovir (800mg 4 times aday from days 7 to 14 after exposure) is recommended. Oral valaciclovir 1,000mg 3 times a daycan 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. o 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 occasions respectively. If the woman presents later than day 7 after exposure, a 7-day course of antiviralscan be started up to day 14 after exposure, if necessary. o 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 acyclovir. Given the short half-life of acyclovir 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. o If a pregnant woman presents with a chickenpox rash, they should be changed to a therapeutic dose (acyclovir 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 hospitalized and given IV acyclovir. **Infants and neonates** o 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 <150mIU/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 o If chickenpox develops despite VZIG, high dose intravenous acyclovir treatment of 20mg/kg every 8 hours for at least 7 days should be started as soon as possible.
Addition of a new section: Management of herpesvirus reactivations in patients with solid	o Acyclovir has long been the primary choice for prophylaxis and treatment of HSV (herpes simplex virus) and VZV (varicella-zoster virus) in immunocompromised patients. o Recommendations include oral acyclovir 400 mg BID or 400 mg QID as prophylaxis for oral HSV disease (AIIr). o Oral valacyclovir can be an alternative (BI), but the best regimen (250 mg BID or 500 mg BID) has not yet been defined. o For patients not tolerating oral medication, intravenous acyclovir 250 mg/m2 TID is suitable

tumors and hematologic malignancies: update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO) on herpes simplex virus type 1, herpes simplex virus type 2, and varicella zoster virus **(2022)**[12]	(AIIr). o Long-term (6 to 12 months) oral administration of acyclovir, valacyclovir, or famciclovir suppresses genital herpes in patients with frequent recurrences (suppressive therapy). Acyclovir 400 mg BID is widely used and tested (AI); valacyclovir 500 mg BID and famciclovir 500 mg BID are approved for this indication in immunocompromised patients (BIIt). o Acyclovir has demonstrated efficacy in reducing clinical VZV reactivation and increasing survival in HSCT (hematopoietic stem cell transplant) recipients. o Antiviral prophylaxis with acyclovir is standard of care in allogeneic and autologous HSCT recipients and non-HSCT patients undergoing tumor treatment. Recommendations include oral acyclovir to reduce clinical VZV reactivation, with dosages ranging from 400 mg once daily to 400 mg TID (AII). o Valacyclovir may also be effective, but evidence is limited (CIIu). o For patients not tolerating oral medication, intravenous acyclovir is suitable, but evidence on the most appropriate dosage is lacking (BIIt). o It's essential to note that all three nucleoside analogues (acyclovir, valacyclovir, famciclovir) require dose adjustment in patients with renal impairment. **Vaccination:** o Highly effective vaccines are available for VZV. The live-attenuated varicella virus (vOKA) has been introduced during childhood for primary prophylaxis against VZV. o Two types of herpes zoster vaccines, Zostavax® (live-attenuated, contraindicated in immunocompromised individuals) and Shingrix® (adjuvanted recombinant subunit), have been studied and approved, with Shingrix® being the preferred option for immunocompromised individuals. o The recombinant zoster vaccine Shingrix® is recommended for the prevention of herpes zoster and post-herpetic neuralgia in adults aged 50 years or older and adults at an increased risk of herpes zoster. o Despite the preliminary nature of data on clinical efficacy in certain malignancies and limited information on long-term protection rates, vaccination with Shingrix® is recommended due to its safety and immunogenicity. However, for specific high-risk patient

groups, such as those with hematologic malignancies, it is suggested to consider additional acyclovir prophylaxis until more comprehensive data, especially from comparative trials between vaccination and pharmacological prophylaxis, become available.

- Increased adoption of Shingrix® in immunosuppressed patients, if clinically proven effective, is anticipated to reduce the reliance on pharmacological prophylaxis, pending further evidence.

Clinical situation	Intention	Intervention	SoR	QoE	Comments
Patients with solid tumors and systemic therapy (in general; for specific risks see below) Patients with HNSCC, treated with radio chemotherapy	To prevent HSV/VZV reactivation	Acyclovir	D	III	Low risk of reactivation
Patients with HNSCC, treated with radio chemotherapy	To prevent HSV stomatitis	**Acyclovir**	**C**	**IIr**	
Patients with malignancies, taking corticosteroids in high doses long term (> 10 mg PEQ per day for 14 days or longer)	To prevent herpes zoster	**Acyclovir**	**C**	**IIu**	Persisting risk for several months after corticosteroid has been stopped

Clinical situation	Intention	Intervention	SoR	QoE	Comments
Patients with AML/high-risk MDS, planned for intensive therapy	To prevent HSV stomatitis and other clinical manifestations of HSV	Acyclovir, valacyclovir[a]	**B**	**IIr**	For remission induction chemotherapy
	To prevent herpes zoster (and other clinical reactivation of VZV)	Acyclovir, valacyclovir[a]	**B**	**IIr**	
Patients with ALL	**To prevent HSV stomatitis and other clinical manifestations of HSV**	Acyclovir	**B**	**I**	Particularly in patients with APL treated with arsenic trioxide
	To prevent herpes zoster[b]	Acyclovir	**B**	**III**	While on treatment
Patients with MPN, treated with ruxolitinib	To reduce HSV disease	Acyclovir	**C**	**IIu**	
	To prevent herpes zoster[b]	Acyclovir	**B**	**IIru**	

aValacyclovir may be used as well, although trials are limited compared to acyclovir (see text).
bData are mainly available for herpes zoster; evidence for other clinical reactivations of VZV is unclear.

Clinical situation	Intention	Intervention	SoR	QoE	Comments

Patients with non-Hodgkin lymphoma, treated with immune-chemotherapy[a]	To reduce HSV/VZV disease To reduce mortality	Acyclovir (valacyclovir)[b] Acyclovir	B C	IIu IIah	Persisting risk for several months after therapy Together with cotrimoxazol, in patients aged>60 years
Patients with Hodgkin's disease[a]	To prevent herpes zoster	Acyclovir (valacyclovir)[b]	C	III	
Patients with CLL receiving immune-chemotherapy	To reduce HSV/VZV disease	Acyclovir (valacyclovir)[b]	B	IIuh	Persisting risk for several months after therapy (see text)
Patients with CLL (and other Non-Hodgkin lymphoma) receiving BTK or BCL2 inhibitors[a]	To prevent herpes zoster (to reduce VZV/HSV disease)	Acyclovir (valacyclovir)[b]	C	IIu	Of beneft particularly in advanced lines of therapy
Patients with CLL (and other Non-Hodgkin lymphoma) receiving idelalisib	To reduce HSV/VZV disease	Acyclovir	B	III	High general risk of opportunistic infections, persisting for several months after therapy
Patients with MM, receiving bortezomib	To reduce VZV disease[c]	Acyclovir, valacyclovir	A	IIu	[d]

Patient with MM receiving carfilzomib	To reduce VZV disease[c]	e.g., acyclovir	B	IIu	[d]
Patients with MM receiving ixazomib	To reduce VZV disease[c]	e.g., acyclovir	A	IIu	[d]
Patients with MM receiving lenalidomide	To reduce VZV disease[c]	e.g., acyclovir	A	IIh	[d]
Patients with MM receiving daratumumab	To reduce VZV disease[c]	e.g., acyclovir	C	IIh	[d]
Patients with MM receiving elotuzumab	To reduce VZV disease[c]	e.g., acyclovir	C	IIt	[d]
Patients with MM receiving conventional-dose chemotherapy[e] or other targeted agents[a]	To reduce VZV disease[c]	e.g., acyclovir	C	IIt	[d]

a Individual risk assessment is recommended: The following risk factors have been described in patients with non-Hodgkin lymphoma or CLL: age>60 years, concomitant treatment with high doses of corticosteroids (cumulative PEQ dose >2500 mg/m2 BSA), advanced line of therapy, type of therapy (bendamustine, maintenance by anti-CD20 monoclonal antibodies), history of febrile neutropenia, and history of HSV/VZV reactivation. The risk factors may also help in decision making for antiviral prophylaxis in patients with multiple myeloma.

b Valacyclovir has been used as well, but evidence is less clear.

c VZV disease: data mainly refer to herpes zoster. Data on HSV disease are rarely reported

d Reactivation risk by a single agent is difficult to determine, because combinations were mainly

	used; prophylaxis in trials was frequently open (“might be considered or recommended”), and duration of prophylaxis has not been determined. **e** Excluding patients with multiple myeloma treated with high-dose chemotherapy and autologous HSCT. For those antiviral pharmacological prophylaxis is highly recommended: A IIt (to prevent HSV reactivation) and A IIu (to prevent VZV reactivation). **Treatment** o The decision to initiate treatment is typically based on clinical diagnosis, often preceding or occurring without confirmation through virus detection. o Treatment choices are influenced by factors such as (a) the type and severity of HSV or VZV reactivation, (b) the patient's clinical condition, and (c) the degree of immunosuppression. o Oral administration is suitable for localized diseases with minor symptoms and mild immunosuppression. In such cases, alternatives to oral acyclovir (400 mg five times per day for localized HSV disease or 800 mg five times per day for herpes zoster) include valacyclovir (1000 mg three times per day) and famciclovir (500 mg twice or three times per day for herpes genitalis or herpes zoster). o However, data are primarily derived from immunocompromised patients with HIV. The duration of therapy is typically 7 to 10 days. o Close clinical monitoring is crucial during therapy, and a switch to intravenous acyclovir is recommended if signs of cutaneous dissemination, involvement of the central nervous system, or other organ complications emerge. o For patients with severe immunosuppression and a high risk of complications, initial intravenous therapy is advisable, and early effective therapy is essential to minimize complication rates. Intravenous acyclovir is administered at 5 mg/kg body weight three times per day for localized HSV disease and 10 mg/kg body weight three times per day for disseminated, cerebral, or visceral disease of HSV and VZV, as well as for herpes zoster. The treatment duration for disseminated disease, cerebral, and visceral disease is at least 14 days. o In general, treatment recommendations for patients with malignancies align with those for the general population, as specific trials for malignancy patients have not been conducted. o It is important to note that brivudin is not approved for immunocompromised patients and is

	contraindicated, particularly in patients treated with 5-fluorouracil or its prodrugs (such as capecitabine, tegafur), due to potential lethal hematologic toxicity.
Addition of a new section: NHSGGC Pediatrics for Health Professionals; Varicella Zoster Infection (chickenpox): management in children **(2022)**[10]	**High risk patient groups requiring admission** The subsequent individuals are susceptible to experiencing severe infection and necessitate hospitalization: 5. Infants aged less than one month 6. Immunocompromised children 7. Children exhibiting ongoing lesion development beyond day 5, posing a risk of disseminated disease 8. Children facing significant complications (bacterial secondary infection, neurological, or respiratory complications) **Antiviral treatment** o In immunocompetent children aged over 1 month and in good health, antiviral treatment is typically unnecessary. o For at-risk children with the potential for moderate disease, consider oral Acyclovir for a duration of FIVE days. o The following categories of children should be administered oral Acyclovir for FIVE days: – Those over 13 years old presenting within the initial 24 hours – Individuals with concurrent severe skin conditions like eczema – Children with underlying pulmonary diseases such as Cystic Fibrosis, chronic lung disease, asthma requiring inhaled steroids, or interstitial lung disease – Children taking aspirin – Those presently receiving short-course or intermittent oral corticosteroids (e.g., 1-2 mg/kg prednisolone) for viral-induced wheezing or asthma exacerbation o It is crucial to counsel families on maintaining adequate fluid intake while the child is on acyclovir. o For the following cases, initiate IV acyclovir following the BNF-c guidelines or refer to the

West of Scotland Neonatal drug monographs for neonates:

- Babies under 1 month: 7 days of treatment
    - Note: Well infants with a low number of lesions, and whose mothers have a history of chickenpox, may not require the full 7 days of treatment. Consultation with Infectious Disease specialists should be sought in such cases after 48 hours of treatment.
- Immunocompromised Children: 7 days of treatment or until no new lesions for 48 hours
- Children still developing new lesions for more than 5 days: Treat until 48 hours after the appearance of the last lesions.
- Children admitted with virally mediated complications or serious bacterial complications with ongoing new lesions.
    - Consider IV acyclovir for severe varicella in children not previously identified as immunodeficient, as this could indicate severe immune compromise.
    - It is important to note that Acyclovir is renally excreted and has been associated with renal impairment, especially in dehydrated patients. Adequate hydration should be maintained, and a low threshold for considering IV fluids is recommended. Accurate fluid balance should be recorded, and U&Es with creatinine should be monitored every 2-3 days or daily in patients with underlying renal dysfunction.

Symptomatic treatment for all Children

- Paracetamol for fever
- Topical calamine can be used but there is no evidence basis, and it can be felt to dry the skin and increase itching
- Antihistamines (e.g chlorphenamine) can be used for itch
- Parents should be advised to keep children's nails short, cover affected skin with loose light clothing and encourage oral fluids
- **NSAIDS (e.g Ibuprofen) should be avoided.**

Post-exposure prophylaxis

- The goal of post-exposure prophylaxis is to safeguard individuals at high risk of severe chickenpox, testing negative for varicella IgG, and meeting the following criteria:
    - **Significant Exposure:** Individuals with substantial exposure to chickenpox or shingles

	during the infectious period. – **Risk-Increasing Condition:** Those with a medical condition that elevates the risk of severe chickenpox. o For a high-risk child of unknown antibody status exposed to chickenpox, urgent antibody status checking is necessary. If there's no known history of chickenpox, prophylaxis should be administered from day 7 to day 14 post-exposure*. In cases suggestive of previous varicella infection, prophylaxis should commence upon obtaining a negative antibody result (VZV IgG <150mIU/ml), with discussions involving the child's overall medical care team. o For patients presenting after day 7 of exposure, a 7-day antiviral course can begin as soon as possible and extend up to day 14 post-exposure if needed. *The day of exposure is defined as the date of rash onset if the index case is a household contact OR the date of the first or only contact for exposure on multiple or single occasions, respectively. o Patients receiving regular intravenous or subcutaneous immunoglobulin do not require additional prophylaxis. In cases of uncertainty regarding whether a child should receive post-exposure prophylaxis, contact their relevant medical team. Rheumatology has separate guidance and should be directly consulted for advice. o Both Varicella immunoglobulin (VZIG) and oral acyclovir are suitable for prophylaxis. However, the UK Health Security Agency (formerly Public Health England) and Public Health Scotland now recommend that most patients (excluding neonates exposed within 7 days of delivery) should be managed with a high dose of oral acyclovir for 7 days, starting on day 7 post-exposure. o In cases where a patient presents after day 7 of exposure, a 7-day course of antivirals can be initiated as soon as possible and continued up to day 14 post-exposure, if necessary. o Patients may still contract chickenpox despite prophylactic treatment and should be advised to promptly seek medical attention if symptoms develop. o In situations where concerns exist about malabsorption or oral antivirals are contraindicated, VZIG should be considered and administered as soon as possible within 7 days of exposure. For patients presenting after 7 days, there may still be a benefit in giving VZIG up to 10 days post-exposure. Varicella antibodies should be checked, and VZIG should

	only be given if negative or the result is <150mIU/ml. o If a patient presents following a second exposure, they should be reassessed, and blood should be taken for varicella IgG. If they have not seroconverted, a further course of acyclovir is required (including patients who have just completed a course of antivirals), starting 7 days after the subsequent exposure. Patients who have recently received VZIG and have a second exposure may need a further dose if the first dose was given more than 3 weeks ago. If the exposure was significant, a further dose should be given if within 3-6 weeks following the initial administration of VZIG without further testing. If more than 6 weeks following VZIG, antibody levels should be rechecked, and a decision to treat should be made based on the results. **Post-exposure prophylaxis in neonates** o Infants at the highest risk of severe disease are those born to mothers who contract chickenpox (not shingles) within the period ranging from 7 days before to 7 days after delivery. o For these infants, Intramuscular Varicella Zoster Immune Globulin (IM VZIG) should be administered as soon as possible, either within 7 days of birth or within 7 days of the onset of the disease in the mother if this occurs later. Additionally, for the highest-risk infants whose mothers develop varicella between 4 days before delivery and 48 hours post-delivery, there is a recommendation to consider admission for a 5-day course of intravenous acyclovir prophylaxis. This prophylaxis should commence on day 7 of maternal varicella. **Post-exposure prophylaxis is also advised for the following scenarios:** o Infants of non-immune mothers (Varicella IgG <150mIU/ml) who experience a significant non-maternal exposure within the first 7 days of life. In cases where the mother has no or uncertain history of chickenpox or has received the varicella vaccine, urgent antibody testing of the mother is recommended before treatment, if possible. o Infants (under 1 year) who have remained in the hospital since birth and were born before 28 weeks of gestation or had a birth weight below 1 kg and are non-immune or have a varicella IgG level <150mIU. o Infants with severe congenital or underlying conditions necessitating prolonged intensive or

	special care during the first year of life and who are non-immune or have a varicella IgG level <150mIU/ml. In such cases, oral or intravenous acyclovir can be considered as an alternative to VZIG after exposure. If the infant is over 4 weeks old (regardless of gestation at birth), oral acyclovir is the preferred option unless contraindicated. Acyclovir initiation occurs on day 7 post-exposure. If contraindicated, VZIG should be administered. o It is important to note that approximately 50% of infants given VZIG may still develop chickenpox, but the course is likely to be milder. Parents should be instructed to bring the infant to the hospital if symptoms or signs of chickenpox develop. The incubation period of chickenpox in infants who have received VZIG can extend up to 28 days.
Addition of a new section: Clinical, Cosmetic and Investigational Dermatology; Molluscum contagiosum: an update and review of new perspectives in etiology, diagnosis, and treatment (2019)[13]	o Currently, the appropriateness of active treatment for patients with MC is a subject of controversy, given the self-limiting nature of the infection, the abundance of therapeutic options, and the absence of conclusive evidence defining optimal therapy. o Consensus suggests that treatment is warranted in cases of extensive disease, secondary complications (such as bacterial superinfection, molluscum dermatitis, conjunctivitis), or aesthetic concerns. o For all patients, general measures to prevent MCV spread are recommended. Patients should be advised against scratching or rubbing lesions, and sharing towels, tubs, or bath utensils should be avoided. o Active treatments fall into categories such as mechanical, chemical, immunomodulatory, and antiviral methods. **Mechanical Methods:** o Cryotherapy, administered with a cotton-tipped swab or portable sprayers, has shown efficacy, with complete clearance rates ranging from 70.7% to 100% in various studies. However, drawbacks include the potential for blistering, scarring, and hypo or hyperpigmentation. o Curettage, involving physical lesion removal, has proven effective, with one study reporting a complete clearance of 80.3% after a single session. Pain, bleeding, and scarring are potential side effects. **Chemical Methods:** o Cantharidin, an inhibitor of phosphodiesterase, induces an intraepidermal blister, resulting

	in variable cure rates (15.4% to 100%). Caution is advised in facial and anogenital regions due to the risk of bacterial superinfection. o Potassium hydroxide, dissolving keratin, has shown clearance rates of 58.8% to 64.3%, comparable to other treatments. **Immunomodulatory Methods:** o Imiquimod, an immune-stimulatory agent, has demonstrated mixed efficacy in studies, with potential adverse effects including pain, blistering, scars, and pigmentary changes. Its current status as a therapeutic alternative is controversial. o Other methods include oral cimetidine, interferon alfa, candidin, and diphencyprone. **Antivirals:** o Cidofovir, an antiviral used in immunosuppressed patients, can be administered topically or intravenously, with the latter posing nephrotoxicity risks.
Addition of a new section: Guidelines for the Treatment of Measles by Centers for Disease Control and Prevention of America – November 5, 2020[14]	o Treatment for measles does not involve specific antiviral therapy. Instead, medical care is supportive, aiming to alleviate symptoms and manage complications, especially bacterial infections. o In cases of severe measles in children, particularly those requiring hospitalization, vitamin A treatment is recommended. Immediate administration upon diagnosis and a repeat dose the following day are advised. The recommended daily doses vary based on age: • 50,000 IU for infants below 6 months • 100,000 IU for infants aged 6–11 months • 200,000 IU for children aged 12 months and older **Vaccine Recommendations:** **Children** o The CDC recommends routine childhood immunization with the MMR vaccine, starting with the first dose between 12 and 15 months of age, and the second dose at 4 through 6 years or at least 28 days after the first dose. The MMRV vaccine is also available for children aged 12 months through 12 years, with a minimum interval of three months between doses. **Students at Post-High School Educational Institutions** o Students without evidence of measles immunity at post-high school educational institutions should receive two doses of the MMR vaccine. The second dose should be

	administered no earlier than 28 days after the first dose. **Adults** o Individuals born in 1957 or later without evidence of measles immunity should receive at least one dose of the MMR vaccine. **International Travelers** o People aged 6 months or older traveling internationally should be protected against measles. Recommendations include: • Infants aged 6-11 months: one dose of MMR vaccine • Children aged 12 months or older: documentation of two doses of MMR vaccine, with the first dose administered at 12 months or older and the second at least 28 days later. • Teenagers and adults born in 1957 or later: documentation of two doses of MMR vaccine, with the second dose administered at least 28 days after the first. *Note: Infants receiving one dose of MMR vaccine before their first birthday should follow the recommended schedule for two additional doses (at 12-15 months and 4-6 years or at least 28 days later). Additionally, the MMRV vaccine is available for children aged 12 months through 12 years, with the first dose administered at 12 months or older and the second dose at least three months later. MMRV is not recommended for those older than 12 years of age. **Post-exposure prophylaxis** o Post-exposure prophylaxis (PEP) is recommended for individuals exposed to measles who cannot promptly demonstrate immunity. o To potentially offer protection or alter the disease's clinical course in susceptible individuals, MMR vaccine should be administered within 72 hours of initial measles exposure, or immunoglobulin (IG) within six days of exposure. It is crucial to avoid simultaneous administration of MMR vaccine and IG, as this practice renders the vaccine ineffective. **Isolation** o Isolation measures for individuals infected with measles involve maintaining isolation for a period of four days after the onset of a rash. In healthcare settings, airborne precautions should be strictly followed. o Due to the slight possibility of MMR vaccine failure in healthcare providers exposed to infected patients, all healthcare personnel caring for individuals with measles should adhere

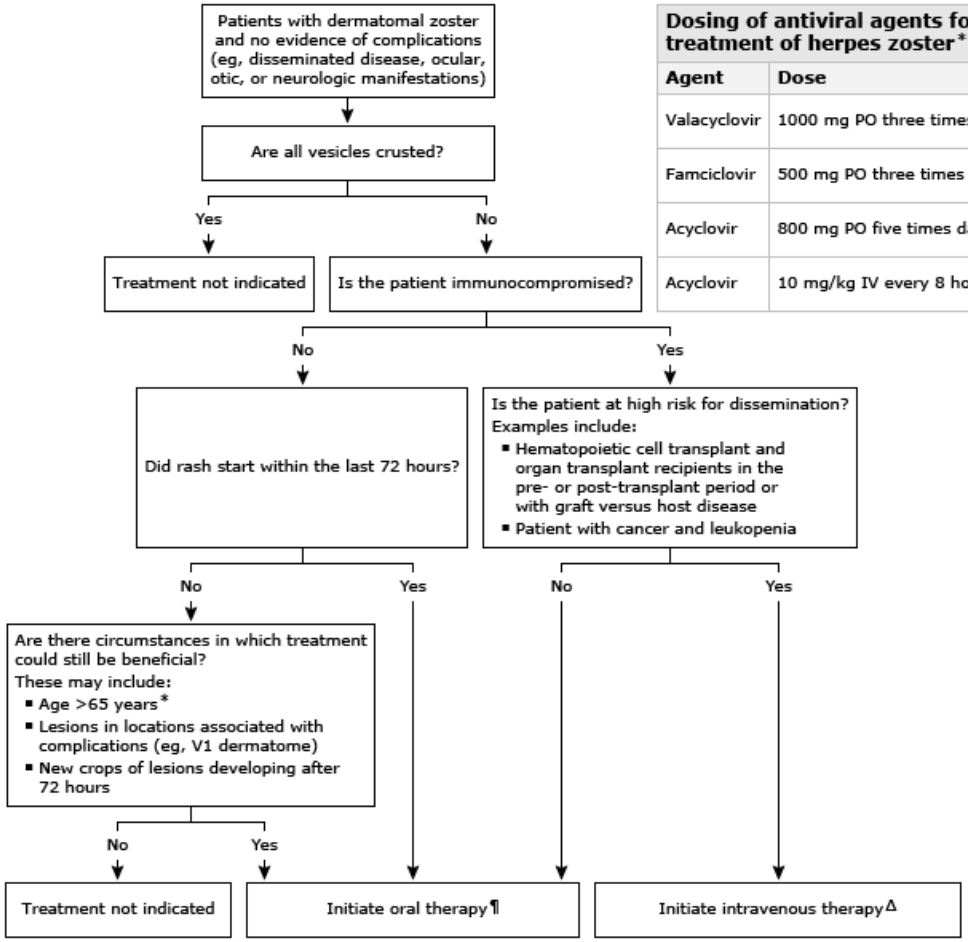
	to airborne precautions. o The recommended placement for patients requiring airborne precautions is in a single-patient airborne infection isolation room (AIIR). o Regardless of presumptive immunity status, all healthcare staff entering the room should use respiratory protection consistent with airborne infection control precautions, such as an N95 respirator or a respirator with similar effectiveness in preventing airborne transmission.

Appendix C. PubMed Search Methodology Terms

The following PubMed Search Methodology was opted:

Query	Filters	Search Details	Results
(((((Skin Diseases, Viral[MeSH Terms]) OR (Viral Skin Diseases[Title/Abstract])) OR (Disease, Viral Skin[Title/Abstract])) OR (Diseases, Viral Skin[Title/Abstract])) OR (Skin Disease, Viral[Title/Abstract])) OR (Viral Skin Disease[Title/Abstract])	Guideline, in the last 5 years	("skin diseases, viral"[MeSH Terms] OR "viral skin diseases"[Title/Abstract] OR (("Disease"[MeSH Terms] OR "Disease"[All Fields] OR "Diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields]) AND "viral skin"[Title/Abstract]) OR "diseases viral skin"[Title/Abstract] OR "skin disease viral"[Title/Abstract] OR "viral skin disease"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]))	4

Appendix D. Viral Skin Infections Treatment Algorithms



Dosing of antiviral agents for treatment of herpes zoster*¶◇

Agent	Dose
Valacyclovir	1000 mg PO three times daily
Famciclovir	500 mg PO three times daily
Acyclovir	800 mg PO five times daily
Acyclovir	10 mg/kg IV every 8 hours

Figure 1. *Initial management of adults with uncomplicated herpes zoster*

This algorithm is intended for adults with localized, uncomplicated herpes zoster
IV: intravenously; PO: orally.

* There is no specific age cut off to decide when someone who presents after 72 hours may benefit from treatment. However, immunity to varicella-zoster virus (VZV) wanes with increasing age and can be severely impaired in those of advanced age.

¶ For nonpregnant patients who warrant oral therapy, we prefer treatment with valacyclovir or famciclovir because of their lower dosing frequency compared with acyclovir. For pregnant patients, we prefer acyclovir since there is the most experience with this medication in pregnancy. Treatment should continue until all lesions have crusted (typically 7 days for immunocompetent patients; 7 to 14 days for immunocompromised patients).

Δ For patients at high risk for dissemination, we initiate intravenous acyclovir. Patients can switch to an oral agent after clinical improvement; treatment should continue until all lesions have crusted (typically 7 to 14 days).

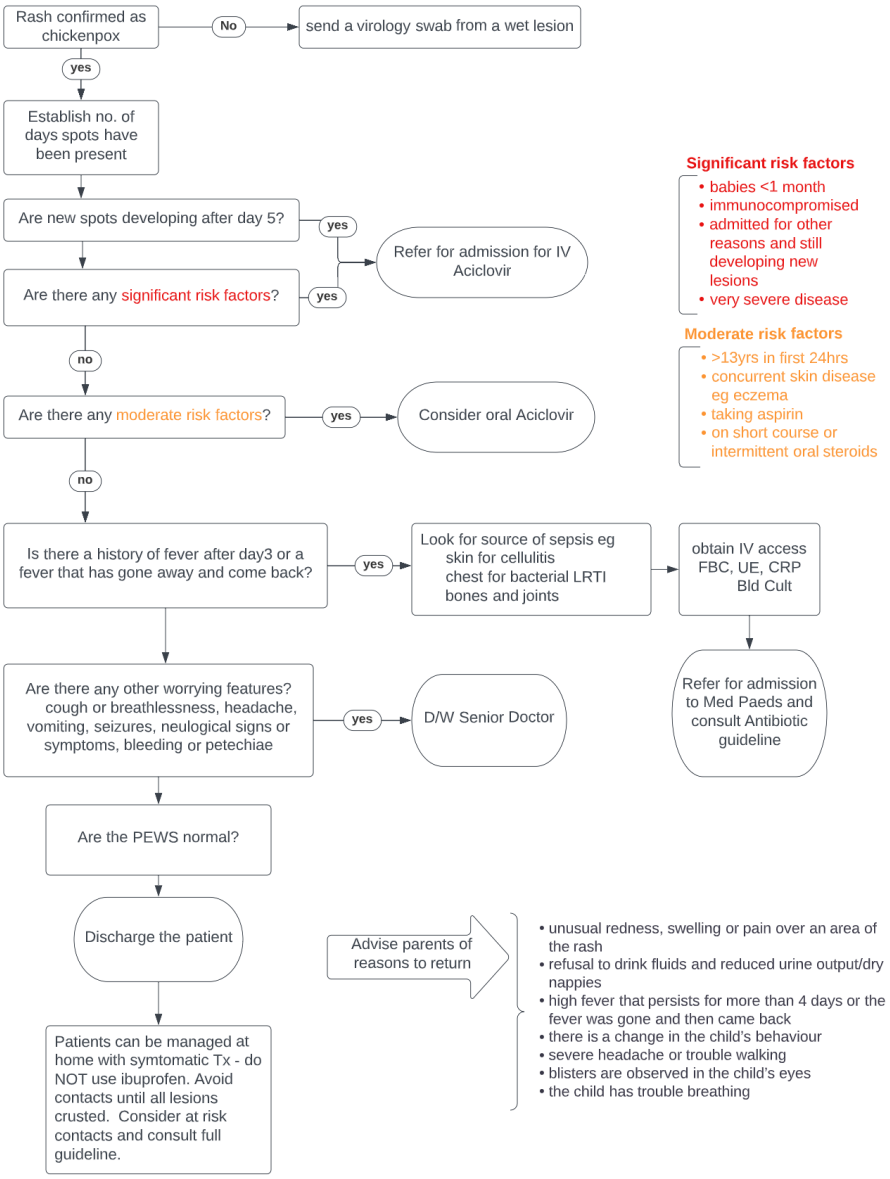


Figure 2. *Varicella zoster infection (chickenpox): management in children*

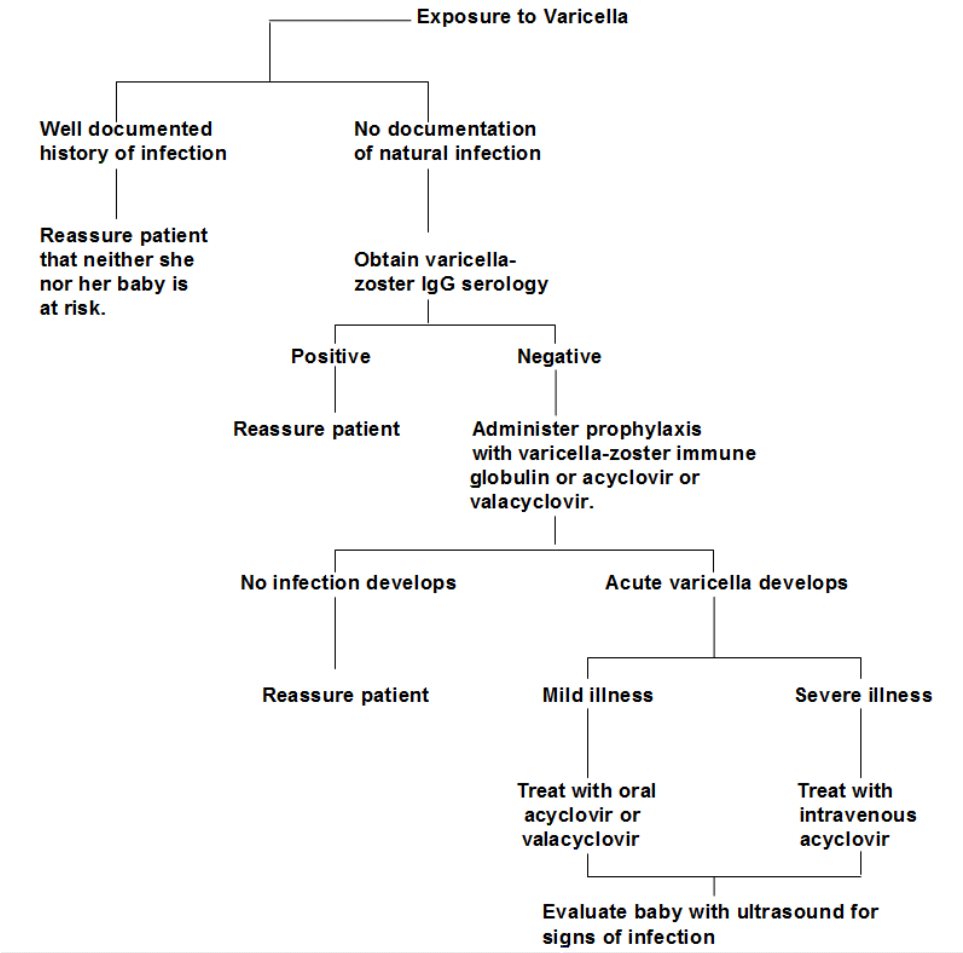


Figure 3. *Diagnosis and management of varicella in pregnancy*

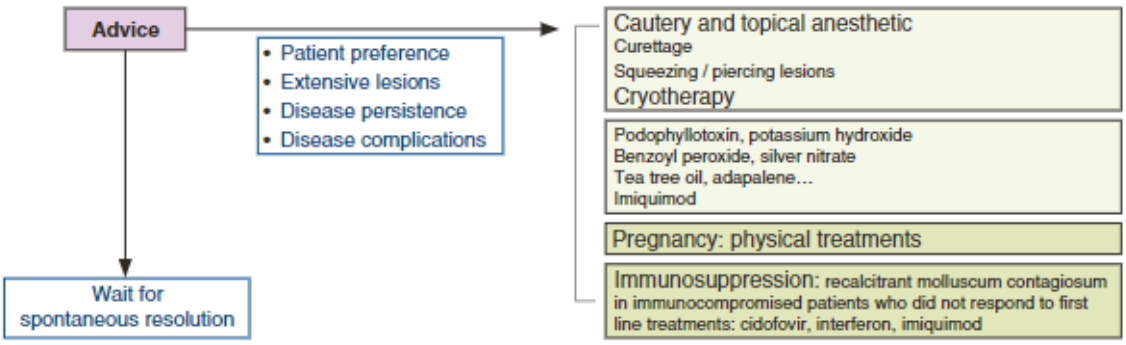


Figure 4. *Management of molluscum contagiosum patient*