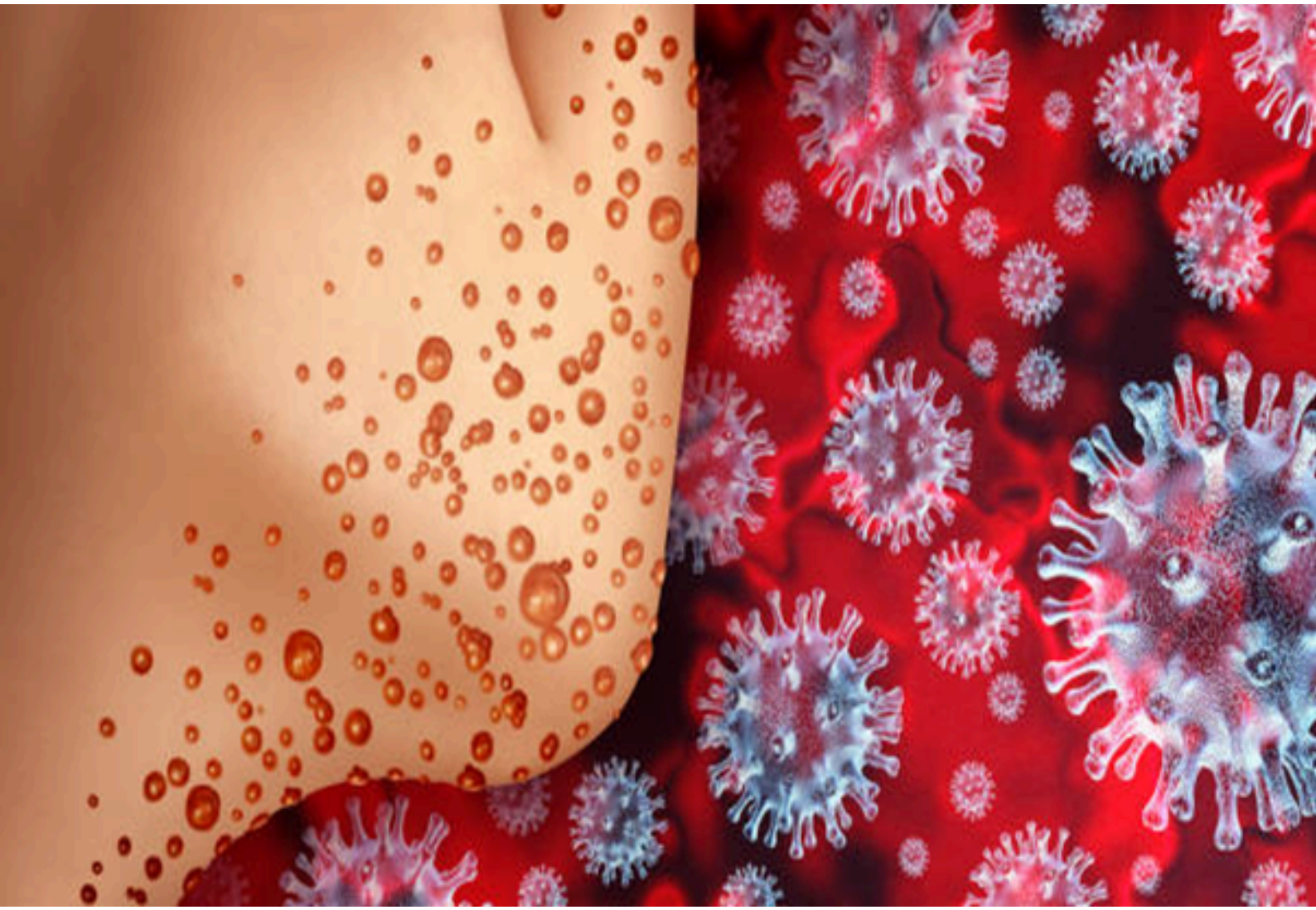
Guidelines for the Clinical Recognition, Diagnosis and Management of Mpox in South Africa



AUGUST 2025

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

TABLE OF CONTENTS

Acknowledgments..... iii
Foreword..... iv
Abbreviations..... v
Executive summary..... vi
Target Audience..... vii
CLINICAL RECOGNITION..... 8
1.1 Case definitions..... 8
1.1.1 Suspected case..... 9
1.1.2 Probable case..... 9
1.1.3 Confirmed case..... 9
1.1.4 Discarded case..... 10
1.1.5 Suspected mpox reinfection..... 10
1.1.6 Probable mpox reinfection..... 10
1.1.7 Confirmed mpox reinfection..... 10
1.1.8 Mpox persistent infection..... 11
1.1.9 Mpox relapse..... 11
1.1.10 Mpox death 11
1.1.11 Definition of a contact..... 11
1.2 Clinical presentation of mpox..... 12
1.2.1 History and physical examination..... 12
1.2.2 Clinical features of mpox..... 13
1.2.3 Atypical presentation of mpox..... 14
1.2.4 Differential Diagnosis..... 16
1.3 case screening and triage..... 17
1.3.1 Screening..... 17
1.3.2 Setting up a screening area..... 17
1.3.3 Triage..... 18
1.3.4 Clinical decision guide..... 18
1.3.5 Admission Criteria..... 20
2. LABORATORY INVESTIGATION OF MPOX..... 21
2.1 Specimens..... 21
2.2 Packaging and shipment of clinical specimens..... 22
2.3 Laboratory testing methods..... 22
2.3.1 Nucleic acid amplification testing and sequencing..... 22
2.3.2 Electron microscopy and histology..... 23
2.3.3 Viral culture..... 23
2.3.4 Serology..... 23
2.4 Access to laboratory testing in South Africa..... 23
3. CLINICAL MANAGEMENT OF MPOX..... 24
3.1 Management of mild or uncomplicated mpox..... 24
3.2 Management of severe mpox..... 25
3.2.1 Definition for severe mpox..... 25
3.2.2 Treatment for severe mpox2..... 25
3.3 Special considerations..... 27
3.3.1 Immunocompromised patients including those living with HIV..... 27

3.3.2 Women and persons who are pregnant or postpartum..... 29
3.3.3 Children..... 29
3.3.4 Breastfeeding..... 29
3.4 General management considerations..... 30
3.4.1 Clinical management of skin lesions..... 30
3.4.2 Management of pain..... 30
3.4.3 Proctitis..... 31
3.4.4 Oropharyngeal lesions..... 31
3.4.5 Ocular manifestations..... 32
3.4.6 Mental healthcare..... 32
3.4.7 Tecovirimat..... 33
3.4.8 Infection prevention and control..... 38
3.4.9 Vaccination..... 40
APPENDICES..... 41
Appendix 1: General guidelines for taking a sexual history..... 41
Appendix 2: Mpox screening tool for healthcare facilities..... 42
Appendix 3: Section 21 Tecovirimat access process..... 43
Appendix 4: Vital signs and clinical features to monitor systematically..... 44
Appendix 5: Clinical management of complications and severe forms of mpox..... 45
Appendix 6: Mpox screening tool for health workers..... 46
Appendix 7: Mpox triage and clinical assessment for suspected and confirmed cases..... 47
Appendix 8: Mpox lesions differential diagnosis..... 48
Appendix 9: Syphilis & HIV Testing and Management during Pregnancy..... 50
Appendix 10: Syphilis Laboratory-Based Testing during Pregnancy..... 51
Appendix 11: Care of skin lesions in mpox infection..... 52
Appendix 12: Pain management in patients with mpox..... 53
REFERENCES..... 51

LIST OF TABLES

Table 1: Clinical Decision Guide..... 19
Table 2: Summary of specimen type and collection materials required for mpox testing..... 21
Table 3: Risk factors and clinical findings described as being associated with severe disease and poor outcomes (based on small, uncontrolled, observational studies)..... 26
Table 4: Proposed weight-based oral dosing and drug food preparation instructions for patients who cannot swallow capsules..... 35

Acknowledgement

We extend our heartfelt gratitude to the contributors from the National Department of Health, the National Institute for Communicable Diseases (NICD), and the World Health Organization (WHO) for their invaluable input in the development of this document. The collective efforts of numerous stakeholders and experts have been instrumental in shaping this guideline.

The National Department of Health recognizes the significant collaboration among provincial health departments and the dedicated individuals who participated in drafting and providing feedback on various iterations of this document. We firmly believe that the successful implementation of the clinical guideline for mpox will enhance case identification, diagnosis, and management of mpox in South Africa.

We would like to extend special thanks to the Mpox Incident Management Team (IMT) for their unwavering support and guidance throughout the development and finalization of this guideline. Our gratitude goes to the co-chairs: Ms Aneliswa Cele and Prof. Helen Rees. We appreciate the contributions from Mr. Wayne Ramkrishna, Ms. Regina Maithufi, Prof. Lucille Blumberg, Dr. Susan Nzenze, Dr. Jaqueline Weyer, Dr. Jeremy Nel, Dr. Arifa Parker, Dr. Nerissa Moodley, Prof. Anisa Mosam, Dr. Steven Wooley, Dr. John Masina, Dr. Jamie Rylance, Dr. Marta Lado, Dr. Janet Diaz, Dr. Rosamund Lewis, Dr. Joseph Wamala, Dr. Charles Mugero, Dr. Takalani Nemungadi, Dr. Sibongile Ntshangase, as well as Dermatology and Infectious Diseases Specialists. Your dedication and support for this guide are highly appreciated.

Finally, the Department acknowledges the Africa Centres for Disease Control and Prevention which has been supporting countries with capacity building, response coordination and resources mobilisation, including establishing an Incident Management Team to support affected countries; whilst the WHO has played an important role in the country's response plan, for surveillance, preparedness, and response, including facilitating access to countermeasures.

Foreword



The ongoing mpox outbreak has highlighted the urgency of implementing effective surveillance, robust response strategies, and community engagement. In this context, the clinical management guideline serves not only as a reference for healthcare professionals but as a framework for fostering collaboration between public health authorities, healthcare providers, community organizations, and affected populations.

As the public health landscape continues to evolve, continuous education and training for healthcare workers are essential to ensure they stay informed about the latest developments in mpox transmission, symptoms, and treatment protocols. Moreover, efforts to raise awareness about safe practices, reduce stigma, and encourage individuals in risk populations to seek care proactively are fundamental to controlling the outbreak and protecting community health.

This guideline also emphasizes the importance of collecting and analyzing data related to mpox cases. Accurate data collection enables healthcare providers and policymakers to understand the outbreak's scope, identify patterns, allocate resources effectively, and implement targeted interventions prioritizing high-risk groups.

Furthermore, the guideline is designed to be adaptable to the unique cultural and social contexts of South African communities, ensuring that cultural sensitivities are respected and integrated into the delivery of health services. It leverages existing community networks while promoting inclusivity and engagement by involving people living with mpox in conversation about care and support.

This guideline should be used with other tools such as the integrated mpox HIV/STI screening tools and vaccination tools.

In summary, the mpox clinical management guideline is a comprehensive resource aimed at equipping healthcare providers with the knowledge and tools necessary to manage and respond to mpox effectively. By prioritizing education, community engagement, and evidence-based practices, we can significantly mitigate the impact of this public health emergency and work towards a healthier future for all South Africans.

Let us commit to a coordinated and compassionate response as we confront the mpox challenge together.



DR SSS BUTHELEZI
DIRECTOR-GENERAL: HEALTH
DATE:

Abbreviations

ADR	Adverse drug reaction
ARDS	Acute respiratory distress syndrome
ART	Anti-retroviral treatment
CDC	Center for Diseases Control
CSF	Cerebrospinal fluid
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
IMT	Incident Management Team
IO	Intraosseous
IPC	Infection prevention and control
IV	Intravenous
MSM	Men who have sex with men
MSSA	Methicillin-sensitive Staphylococcus aureus
MPX	Mpox
MPXV	Monkeypox virus
NAGI	National Advisory Group on Immunisation
NEMLC	National Essential Medicines List Committee
NICD	National Institute of Communicable Diseases
NMC	Notifiable medical conditions
PCR	Polymerase chain reaction
PPE	Personal protective equipment
SAHPRA	South African Health Products Regulatory Authority
SmPC	Summary of product characteristics
STG	Standard Treatment Guidelines (STG)
SUSARs	Suspected unexpected serious adverse reactions
VTM	Viral transport medium
VZV	Varicella zoster virus
WHO	World Health Organization

Executive Summary

Mpox is an emerging zoonotic viral infection which can be transmitted from person-to-person resulting in outbreaks in the human population. The disease is caused by infection with the monkeypox virus (MPXV), an Orthopoxvirus closely related to the variola virus (the causative agent of smallpox, which has been eradicated). The most prominent feature of the disease is the skin rash which is associated with painful lesions similar in appearance to the smallpox rash. Fever and enlarged lymph nodes are frequently reported. The disease is mostly mild requiring little or no medical intervention, but some people affected may develop scarring. Nevertheless, the disease can be severe and, in some cases, fatal, particularly in those with immunodeficiencies and comorbidities (WHO, 2022).

Historically, mpox was rarely reported in persons and the subject of few studies (Dalton, et al. 2023). Much about the epidemiology, ecology and pathobiology of the disease remains unclear. Two clades of MPXV, namely Clade I and Clade II have been identified and circulate respectively in Central and West Africa. Clade I MPXV virus has been associated with more severe clinical outcomes. A second determinant of mpox epidemiology is due to the high level of immunity afforded against mpox through smallpox vaccination.

Worldwide vaccination during the smallpox eradication campaign also contributed to immunity against mpox. Since cessation of smallpox vaccination more than 40 years ago, populations worldwide have grown more susceptible, and most notably among those who had never been vaccinated. Due to cross-protection between orthopoxviruses, smallpox vaccines provide protection from mpox.

In recent years, the number of mpox cases reported in endemic African countries, and notably in the Democratic Republic of the Congo has been rising. In 2017, Nigeria experienced its first major outbreak of human mpox (Yinka-Ogunleye, 2019). In May 2022, mpox appeared suddenly and spread rapidly across Europe, the Americas and then all six WHO regions. This global outbreak has affected primarily gay, bisexual, and other men who have sex with men (MSM) and spread person-to-person through sexual networks. By August 2024, over 120,000 confirmed mpox cases were reported from 120 countries. Clade Ia has circulated in the DRC and several central and west African countries (e.g. Cameroon, CAR, Gabon, RoC) for decades, where children have been disproportionately affected.

Clade Ib appeared in the DRC in September 2024 and spread to Burundi, Kenya, Rwanda and Uganda and cases are occurring in all regions linked to travel from these countries. Predominantly affected are those in high-contact sexual networks, for example sex workers. South Africa has recorded 25 cases of mpox (Clade IIb) as of 23 October 2024, among men, with 60 per cent identifying as MSM. Following six months of zero case reporting, Clade Ib was reported for the first time in South Africa in a traveller who had returned from East Africa. Two clusters of close contacts linked to the index case led to a total of seven (7) cases including two females and child 14 years of age. Thus, from 2024 to 25 March 2025, 32 mpox cases with three (3) deaths have been reported in South Africa (https://www.nicd.ac.za/mpox-updates/).
This document provides guidance for the clinical recognition, diagnosis, and management of mpox cases in South Africa for use by clinicians seeing or treating mpox patients.

Target audience

This document aims to provide interim guidance for healthcare workers in both public and private sectors including clinicians, health facility managers, health workers and IPC practitioners including but not limited to those working in primary care clinics, sexual health clinics, emergency departments, dental practices, infectious diseases clinics, genitourinary clinics, maternity services, pediatrics, obstetrics and gynecology, and acute care facilities that provide care for patients with suspected or confirmed mpox. For ease of use, we refer to patients being assessed and entering the mpox clinical care pathway as suspected cases, which includes both epidemiological groups (suspected cases and probable cases).

Guidelines for clinical care will be updated as further evidence becomes available. Refer to the WHO clinical care link: https://doi.org/10.2471/B09434

In the public sector, mpox cases are managed at tertiary level with support from expert clinicians in accordance with the Standard Treatment Guidelines (STGs).

Refer to the STGs: https://www.health.gov.za/nhi-edp-stgs-eml/

CLINICAL RECOGNITION

1.1 Case definitions

Mpox can affect all ages. It can cause systemic symptoms, a severe or sparse generalized rash, can involve the mucosa, and in the case of sexual transmission can involve the anogenital area. The following generalized/systemic symptoms typically appear within 1–4 days before the rash:

- Fever
- Chills
- Swollen lymph nodes (a key distinguishing feature from similar illnesses like chickenpox)
- Headache
- Muscle aches and backache
- Fatigue or exhaustion
- Respiratory symptoms: sore throat, nasal congestion, or cough

Rash Presentation- the rash is a hallmark of mpox and progresses through several stages:

- Initial appearance: Macules → Papules → Vesicles → Pustules → Scabs
- Lesion characteristics: deep-seated, well-circumscribed, often umbilicated. Lesions may be painful or itchy, and typically appears 1–4 days after systemic symptoms.
- Distribution includes face, extremities (including palms and soles), trunk, oral mucosa, and genital and perianal areas.

Mucosal Involvement

- Oral mucosa: Lesions in the mouth and throat can cause pain and difficulty swallowing.
- Ocular involvement (can be vision-threatening):
    - Conjunctivitis
    - Blepharitis
    - Keratitis
    - Corneal ulcers
    - Periocular skin lesions
    - In severe cases, vision loss.

Anogenital Involvement

In case of sexual transmission:

- Lesions may appear on or around penis, scrotum, labia, vagina, and anus.
- May be associated with pain, proctitis, and rectal bleeding; this presentation has been especially prominent in recent outbreaks.

The case definitions for suspected, probable and confirmed mpox cases as recommended by the World Health Organization (WHO) are summarised here.

1.1.1 Suspected case

i) A person who is a contact of a probable or confirmed mpox case in the 21 days before the onset of signs or symptoms, and who presents with any of the following: acute onset of fever (>38.5°C), headache, myalgia (muscle pain/body aches), back pain, profound weakness, or fatigue.

AND/OR

ii) A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), rectal pain and/or bleeding.

AND

for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture: **varicella zoster (and herpes zoster)**, measles, **herpes simplex**, bacterial skin infections, disseminated gonococcal infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (for example, to plants); nontuberculous mycobacterial lung disease, deep fungal infections and any other locally relevant common causes of papular or vesicular rash.

N.B. It is not necessary to obtain negative laboratory results for listed common causes of rash in order to classify a case as suspected. Further, if suspicion of mpox or MPXV infection is high due to either history and/or clinical presentation or possible exposure to a case, the identification of an alternate pathogen which causes a rash should not preclude testing for MPXV, as co-infections have been identified.

1.1.2 Probable case

A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or anorectal lesions. Ano-rectal lesions can also manifest as ano-rectal inflammation (proctitis), rectal pain and/or bleeding.

AND

One or more of the following:

- has an epidemiological link (connection between cases based on their exposure or contact) to a probable or confirmed case of mpox in the 21 days before symptom onset
- has had multiple and/or casual sexual partners (regardless of sex/gender) in the 21 days before symptom onset
- has a positive test result for orthopoxviral infection (for example, OPXV-specific PCR without MPXV-specific PCR or sequencing).

1.1.3 Confirmed case

A person with laboratory confirmed MPXV infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR) and/or sequencing.

1.1.4 Discarded case

A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPXV. Conversely, a retrospectively detected probable case for which lesion testing can no longer be adequately performed (that is, after the crusts fall off) and no other specimen is found PCR-positive, would remain classified as a probable case. A suspected or probable case should not be discarded based on a negative result from an oropharyngeal, anal or rectal swab or from a blood test alone.

1.1.5 Suspected mpox reinfection 1

- A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a suspected, probable or confirmed case
- It is unclear if the person presented a full clinical resolution of the previous episode.

1.1.6 Probable mpox reinfection

- A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a probable or confirmed case
- Full clinical resolution of the previous mpox episode occurred
- The time between the resolution of the first episode and the onset of new symptoms is less than three months.

1.1.7 Confirmed mpox reinfection.

- A person who currently meets the criteria for a confirmed case of mpox

AND

- Has a documented history of a previous episode of mpox, as a confirmed case
- Full clinical resolution of the previous mpox episode occurred
- The time between the resolution of the first episode and the onset of new symptoms is three months or more
- When possible, strain differentiation is undertaken using genetic sequencing

OR

- Has a probable mpox reinfection (as described above) with significant strain differentiation between the two mpox infections (for example different lineage and descendant lineages) using genetic sequencing.

---

1 Possible explanations for reinfection include unrecognised immunodeficiency, mild initial infection that did not generate mucosal immunity, or differences in mpox viral strains. Clinical features and outcomes of mpox reinfection and infection post-vaccination are less severe than initial infection.
See Kaul D, twice might be possible: Mpox re -infection, NEJM Journal Watch, 2023. April 18

1.1.8 Mpox persistent infection

- Mpox infection without clinical improvement or resolution of symptoms.

1.1.9 Mpox relapse

- Mpox infection that has improved, but not completely resolved, followed by clinical worsening or new mpox symptoms.

Patients with severe immunodeficiency such as in people living with HIV with CD4 counts <200 can be at risk for persistent and/or relapsed MPXV infections.

1.1.10 Mpox death

Mpox death refers to the fatality or loss of life resulting from an infection with the mpox virus**.**
While most mpox cases are mild and resolve without complications, severe cases, especially in vulnerable individuals like children, pregnant women, and those with weakened immune systems, can lead to serious complications and death.

1.1.11 Definition of a contact

A person who has been exposed to a suspected, probable, or confirmed mpox case during the infectious period (A person is infectious from time of the onset of first symptoms and ending when all scabs have fallen off), and who has one or more of the following exposures:

- direct skin-to-skin, skin-to-mucosal, or mouth-to-mucosal physical contact (such as touching, hugging, kissing, intimate oral or sexual contact)
- indirect contact with materials contaminated by the case, such as clothing or bedding, including material dislodged from bedding or surfaces during handling of laundry or cleaning of contaminated rooms (Refer to IPC guidelines in health settings)
- prolonged face-to-face respiratory exposure in close proximity through close and prolonged conversation with a symptomatic mpox case, especially if they have visible mpox ulcers
- respiratory exposure (i.e., possible inhalation of) or eye mucosal exposure to lesion material (e.g., scabs/crusts) from an infected person
- the above also apply for health workers potentially exposed in the absence of proper use of appropriate personal protective equipment (PPE) refer to IPC guidelines in health settings)
- transmission during pregnancy through the placenta or during delivery.

IPC considerations for confirmed cases with mpox

Contact and droplet precautions be implemented for any confirmed patient with mpox. In addition to contact and droplet precautions, respirators should be used.

Key issues:

- Patients should be managed in a well-ventilated room, ideally with a dedicated bathroom or toilet. If not possible, cohort patients with similar symptoms, maintaining a distance of at least 1 m between patients.

- Isolation room/area should have signage posted at the entrance indicating contact / droplet precautions
- ·Wearing of PPE including gloves, gown, a surgical mask is adequate. However, if using aerosol generating procedure, wear a respirator (e.g., N95, FFP2) and eye protection.
- Use dedicated footwear that can be decontaminated; disposable shoe covers are not recommended.
- Health workers should be trained on procedures for safe donning and doffing of PPE.
- Avoid unnecessary movement of patients. If the patient must be moved or transported within or beyond the facility, ensure transmission-based precautions are maintained, place a well-fitting medical mask on the patient and cover lesions (provided the patient is able to tolerate)
- The receiving facility/ward/unit should be aware that transmission-based precautions are required and, pending arrival, the need to prepare the isolation or designated area.
- Precautions should remain in place until lesions have crusted, scabs have fallen off and a fresh layer of skin has formed underneath.
- Severe cases (including immunosuppressed) who may experience prolonged viral shedding from the upper respiratory tract may require clinical evaluation to determine when transmission-based precautions may be discontinued.

Airborne precautions must be implemented if aerosol-generating procedures (AGPs) are performed.

I**mportant:** Perform AGPs in a well- ventilated, single-patient room with the door closed. Health workers should wear a respirator (e.g., N95, FFP2) as well as eye protection, a gown and gloves when performing AGPs

1.2 Clinical presentation of mpox

1.2.1 History and physical examination

Clinicians should conduct a thorough patient history to assess possible mpox exposures or epidemiologic risk factors. Mpox is usually transmitted through close, sustained physical contact and has been almost exclusively associated with sexual contact in the multi-country outbreak. It is critical that clinicians take a detailed sexual history of the patient with suspected mpox (see Appendix 1). Also, consider other STIs, see Appendix 2 (screening tool).
If mpox is suspected, the health worker must don PPE as per infection prevention and control (IPC) guidelines and perform a complete physical examination. The examination should include a thorough skin and mucosal (e.g. oral, genital, and anal) examination for the characteristic vesicular-pustular rash of mpox. This allows the clinician to detect lesions of which the patient may be unaware.

Mpox should be considered when a clinician is trying to determine the **cause of a diffuse or localised rash.**

1.2.2 Clinical features of mpox

Mpox can cause a range of clinical signs and symptoms. The illness typically lasts two to four weeks. The severity of illness can depend upon the initial health of the individual and the route of exposure. People who are immunocompromised, including those living with HIV who have low CD4 counts, are vulnerable to severe infection. The Clade II genetic group, which is the clade involved in the current multicounty outbreak, is generally associated with milder disease and fewer deaths than the Clade I virus currently circulating in central Africa.
Clade 11 may be complicated in PLHIV not on ARVS.

The **incubation period** for mpox is three to 21 days. During this time, no symptoms are observed.

The **initial phase** of clinical illness typically lasts one to five days, during which time patients may experience fever, headache, back pain, muscle aches, lack of energy and lymphadenopathy.

This is followed by a **second phase**, which typically occurs one to three days after fever subsides with the appearance of a rash which can be dense or sparse. The rash presents in sequential stages – macules, papules, vesicles, pustules, umbilication before crusting over and desquamating over a period of two to three weeks (Figure 1). The lesions range in size from 0.5 to one centimetre in diameter and from a few to several thousand in number. Lesions are firm or rubbery, well-circumscribed, deep-seated, and often develop umbilication (resembles a dot on the top of the lesion). The eruption tends to be centrifugal, starting on the face and extending towards the palms and soles of the hands and feet, and can involve the oral mucous membranes, conjunctiva, cornea and/or genitalia. Oral ulcers are common and may affect a patient's ability to eat and drink leading to dehydration and malnutrition. Rectal swelling and tenesmus are found in some cases. During the multi-country outbreak lesions have often been localised on the genitalia, the peri-anal area and mouth. Inflammation of the pharyngeal, conjunctival and genital mucosa may also occur. Severe penile oedema and distortion may occur. Pain may be severe and has been a primary reason for hospitalisation during the multi-country mpox outbreak.

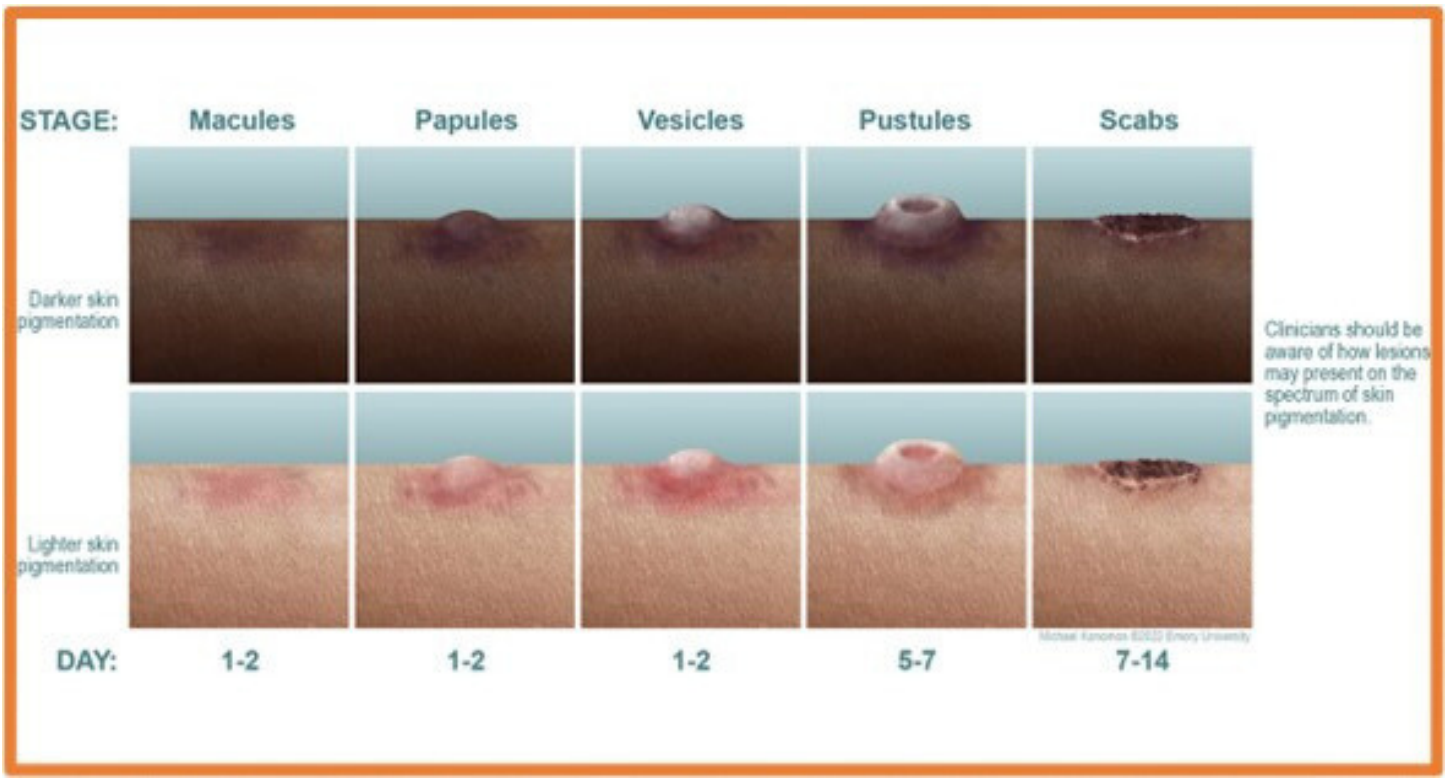


Figure 1. Disease progression by rash stage

1.2.3 Atypical presentation of mpox

Though uncommon, patients with mpox may develop severe and life-threatening complications. For example, the confluence of skin lesions is susceptible to bacterial skin and soft tissue infections such as cellulitis, abscesses, necrotising soft tissue infections requiring meticulous local wound care; subcutaneous accumulation of fluid in the crusting phase leading to intravascular depletion and shock; and exfoliation resulting in areas of skin that may require surgical debridement and grafting.

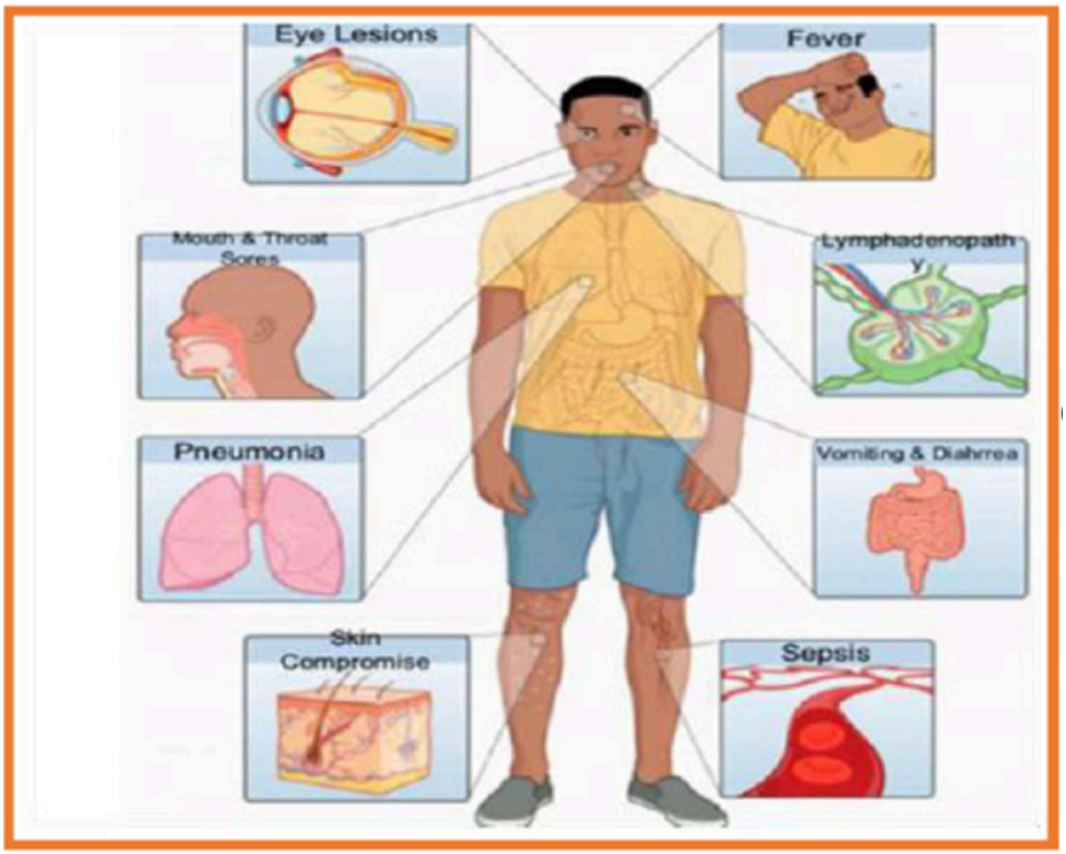


Figure 2. Extracutaneous manifestations of mpox

Non-typical presentations of the disease have been reported among individuals:

- Anal pain and rectal bleeding
- Ocular lesions (scarring, reduced skin pigmentation, blindness)
- Sudden (fewer or even single) rashes on any part of the body
- Close mimic of many STIs: since mpox can present with genital ulcers or a macular rash on the palms and soles, other sexually transmitted infections should be considered (e.g., secondary syphilis, lymphogranuloma venereum, chancroid)

Other rare complications include severe pneumonia and respiratory distress, corneal infection which may lead to vision loss, loss of appetite, vomiting and diarrhoea which may lead to severe dehydration, electrolyte abnormalities and shock, cervical lymphadenopathy which may lead to retropharyngeal abscess or respiratory compromise, sepsis, septic shock, and encephalitis and death (see Appendices 4 and 5 for clinical monitoring and management of severe cases of mpox). Post mpox scarring has been noted as a possible complication and may be prevented or reduced by good wound care, avoiding scratching lesions and applying a thin layer of ointment over affected areas (see Figure 2). Consult with a dermatologist for severe scarring. Scarring leads to stigmatisation of patients post-recovery.

1.2.4 Differential diagnosis

The mpox rash at different stages of evolution, may resemble other infectious diseases or other conditions, including:

- Varicella zoster virus (VZV, chickenpox)
- Herpes simplex virus (HSV)
- Primary or secondary syphilis
- Disseminated gonococcal infection
- Hand, foot and mouth disease,
- Chancroid
- Lymphogranuloma venereum
- Granuloma inguinale
- Molluscum contagiosum
- Measles
- Scabies
- Rickettsiosis
- Chikungunya, Zika virus, dengue fever or other arboviral disease,
- Vasculitis and other bacterial skin and soft tissue infections
- Nontuberculous mycobacterial infections
- Deep fungal infections
- Disseminated cryptococcosis skin lesion under some circumstances
- Other locally relevant common causes of papular or vesicular rash.

The differential diagnosis of mpox includes measles and chickenpox, with mpox typically presenting with deep-seated, umbilicated lesions in a single stage of development and associated lymphadenopathy, whereas chickenpox lesions are superficial, appear in multiple stages, and are more concentrated on the trunk, and measles is characterized by a maculopapular rash, Koplik spots, and a lack of vesicular lesion.

Often the rash caused by VZV may be confused with mpox but can be distinguished as the rash in varicella generally progresses quicker, is more centrally located than the centrifugal distribution of mpox, is in multiple stages of development (rather than the same stage as typically seen in mpox) and patients usually do not have lesions on their palms and soles. Additionally, patients with VZV typically do not have lymphadenopathy, which is often found with mpox. Adult patients or persons of any age who are immunocompromised with suspected varicella should receive acyclovir. Mpox lesions are frequently painful. Chicken pox is associated with pruritic lesions. See appendix 8 for further illustration on differential diagnoses for mpox.

It is important to consider the most likely cause of the rash and most appropriate management since mpox is not commonly reported in South Africa, and the likelihood of exposure, epidemiology of the disease and risk factors in each patient presenting with rash.

1.3 Case screening and triage

1.3.1 Screening

Screening is a strategy used in a population to identify people who could potentially have a disease based on specific signs or symptoms. It is based on a thorough interview and observation of the patient, including history of current symptoms, contact history and local epidemiology.

Screening is best performed at the first contact with the patient, preferably at the entrance of the facility. All persons accessing the facility including health care workers, patients, visitors, survivors, etc. should go through systematic screening using screening tools (appendix 2 and 6).Despite a patient screening negative for mpox, health care workers in the different department of the health facility e.g. laboratory, radiology, antenatal, OPD, etc. are encouraged to continue screening all patients that access their departments as the condition of the patient may change and more signs and symptoms of these diseases manifest or more information made available by the patient that may make them a suspect. Once admitted on the wards, monitoring should be conducted on each shift i.e. 3 times a day (morning, afternoon and evening) using patient monitoring tool (Appendix 2 and 6).

1.3.2 Setting up a screening area

The physical setup for the screening area always assures 1–2 meter distance between the screener and the patient. The health care worker side of the screening area should be set up with a table and chair, hand hygiene facilities, pens, screening tools e.g., screening forms or registers, screening algorithms, and infra-red thermometer. To reinforce practices, job aides such as posters on signs and symptoms, updated case definitions and IPC should be placed within the screening area.

No PPE is required if the 1–2 meter distance between patient and health care worker is maintained. The patient side of the screening area should be set up with hand washing facilities, waiting patient chairs placed at least 1 meter apart, waste bins with bin liners and digital thermometers if infrared thermometers are not available.

The patient can use the digital thermometer to measures his or her own axillary temperature (or their child's) and reads it aloud or shows the reading to the screener. The thermometer can be cleaned and disinfected with 0.5% chlorine between uses with different patients in the screening area. Ensure that cleaning and disinfection on the patient side of the screening area is done in between patients or when spills occur by someone putting on full PPE.

To reinforce precautionary measures including IPC measures, pin visual aids/ posters for IPC, risk communication and direction of flow of person being within the screening area on the patient side.

Signs and symptoms of illness that should be screened for include acute onset of fever (>38.5°C), headache, muscle pain/body aches, back pain, profound weakness, or fatigue, acute skin rash, mucosal lesions, swollen lymph nodes.

NOTE:

Patients who meet the case definition should:

- Enter the mpox clinical care pathway
- Be given a well-fitting medical mask and ask to sanitize their hands
- Be isolated in a well-ventilated single room
- If a well-ventilated room is not available, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation (at least 1meter between patients).

1.3.3 Triage

Triage should be promptly implemented/ conducted to prioritize individuals with critical care needs and efficiently manage limited resources.
Triage is a process of sorting patients into categories based on their need for time sensitive treatment.

Triage identifies patients who require immediate medical intervention and those who can safely wait.

Once the patient is screened, triage should occur inside the isolation area (for patients who screen positive) or similar area close to the entrance of the health facility.

Triage should be done using the mpox triage and clinical assessment for suspect and confirmed cases (Appendix 7).

1.3.4 Clinical decision guide

To assist with decision making, refer to Table 1 below and the mpox screening tool in Appendix 2.

Table 1: Clinical Decision Guide

Clinical Questions	**More supportive of mpox***	**Less supportive of mpox**
Did the patient have a prodrome?	**Yes**: Recent cases have presented without an obvious prodrome. However, a patient with a strong epidemiological link **PLUS,** prodromal symptoms might increase suspicion of mpox. Notably, lymphadenopathy is a distinguishing feature of mpox.	**No**: Recent cases have presented without an obvious prodrome. A patient with an epidemiologic link without prodromal symptoms might decrease suspicion of mpox. Close monitoring should occur for development of a rash or other symptom.
Did the patient develop a rash?	**Yes**: Most cases are expected to have developed a rash at some point in their course.	**No**: Some cases have developed anorectal pain, tenesmus or bleeding, from less- or non-visible perianal lesions.
Site of rash?	**Uncertain:** Classically, mpox rashes have started in the face and extremities then spread to rest of body. In recent cases, rash has often begun in mucosal areas (e.g., genital, perianal, oral mucosa) and in some patients, the lesions have been scattered or localised to a specific body site rather than diffuse and have not involved the face or extremities.	**Uncertain**: Classically, mpox rashes have started in the face and extremities then spread to rest of body. In recent cases, rash has often begun in mucosal areas (e.g., genital, perianal, oral mucosa) and in some patients, the lesions have been scattered or localised to a specific body site rather than diffuse and have not involved the face or extremities.
What is the rash appearance?	Deep-seated and well-circumscribed lesions, often with central umbilication. Lesions progress through specific sequential stages, sometimes rapidly—macules, papules, vesicles, pustules, and scabs.	Other presentations of rashes and rashes that do not progress. Remember, rashes in certain stages can be mistaken for other common rash aetiologies, including STIs such as syphilis, herpes, etc.
Is the rash painful?	**Yes:** Mpox rash is sometimes very painful (or pruritic) and is often a reason people seek evaluation and/or treatment.	**No**: Rashes such as those associated with HSV can be painful however other STIs such as syphilis are not typically painful.
Did the patient test positive for other rash aetiology?	**No**: Negative test for other aetiologies that cause rash that appear similar to that of mpox (e.g., VZV, HSV, syphilis) does not rule out mpox entirely. Co-infections with other STIs have been seen with mpox.	**Yes**: Positive test for other rash aetiology, especially one that cause rashes that appear similar to mpox. Co-infections with STIs, particularly syphilis, have occurred in recent cases, so a positive test does not rule out mpox.

7. Was there contact with a known or suspect mpox case?	· Contact with lesions or bodily fluids · Sexual contacts · Household contacts · Prolonged (3+ hours) unmasked contact within six feet	· Masked contact within 1.8meters · Contact with lesions/bodily fluids while wearing PPE · Shared airspace contact while at least six feet apart
8. Did the patient recently participate in gatherings involving sex, especially with multiple sex partners? Or did the patient participate in intimate contact at venues where there is sex on premises such as bathhouses or saunas?	**Yes**: There have been a number of cases and contacts that were associated with sex or extended physical contact in sex-related events, in bathhouses/saunas, and/or with multiple sex partners.	**No**: No participation or contact with someone who has participated in these activities or attended these venues/events is less suggestive of mpox.
9. Is the patient part of a social group known to have high mpox incidence or vulnerability?	**Yes**: The majority of cases seen in this outbreak have been in men or transgender persons who have sex with men, however, anyone can get mpox.	**No**: No known linkage to a more vulnerable group or any reported high-risk social or sexual behaviours would be less suggestive of mpox.
10. Did the patient recently (within last 21 days) travel to countries/regions where Mpox is known to be spreading?	**Yes**: The index case reported in February 2025 had travel history to country in Eastern Africa, one of the sub-regions where wide transmission of Mpox Clade 1b continues to be reported, both male and female have been affected including children.	**No**: No report of known history of contact with someone who is affected or report of participation in high-risk social or sexual behaviours from country visited.

*While some of the listed factors more strongly suggest an underlying mpox aetiology, no one answer is absolute in determining whether to suspect mpox; instead, the collective responses and overall clinical picture should be considered. Rash associated with lymphadenopathy is strongly suggestive of mpox.

1.3.5 Admission Criteria

- For clinical advice, contact the NICD clinical hotline 0800212552.

2. LABORATORY INVESTIGATION OF MPOX

Any individual meeting the case definition of a suspected case of mpox should be offered testing. The decision to test should be based on both clinical and epidemiological factors, linked to an assessment of the likelihood of infection and the risk of further spread. The rash that develops in mpox may resemble other infectious diseases or conditions, making it challenging to differentiate mpox solely based on clinical presentation (see Appendix 8). It is therefore important to consider other potential causes of discrete skin lesions or a disseminated rash.

In addition to the primary laboratory test of PCR for detecting MPXV, clinicians are encouraged to request for laboratory investigations for other comorbidities like HIV and viral load, testing for other potential co-infections like STIs including syphilis or herpes (see Appendix 9-10).

2.1 Specimens

The recommended specimen type for laboratory confirmation of mpox is skin lesion material, including swabs of lesion surface and/or exudate, or lesion crusts (see Table 1). Blood specimens are generally not useful for diagnosis of acute illness, unless this is taken to rule out other infections.

How to collect the specimens:

- Use appropriate PPE as per IPC protocol for mpox.
- Swab the lesion vigorously (but without causing injury), to ensure adequate transfer of material to the swab.
- Swabs can be transported dry in capped tubes or placed in viral transport media (VTM).

Mpox is diagnosed by polymerase chain reaction (PCR) test for the MPXV on a swab taken from one or more vesicles or ulcers (See Table 2).

Table 2: Summary of specimen type and collection materials required for mpox testing

Specimen type	Collection materials	Comments
Skin lesion material: **Swabs of lesion/s*** Lesion roof/s, and/or lesion crust/s Aspirates of lesion fluid (not recommended, but may be submitted) **Collect specimen by vigorously rubbing the swab over the lesion surface (without causing injury)*	Swabs (for example, Dacron or polyester flocked swabs) can be submitted dry (in capped tube) or in viral transport media. *Preferably, avoid "culture swabs" which is transported in Amies transport media.*	Swabs can be collected from different lesions. Swabs collected from different lesions may be stored in a single tube if so required.

Based on clinical assessment, also screen/test for possible differential diagnosis (see Appendix 8). This can include STIs (that is, HIV, syphilis, gonococcus/chlamydia) in accordance with national guidance for STI screening/testing. Several case series have found concomitant HIV in ~40 per cent and other STIs in ~30 per cent; as a result the integrated mpox screening tool was developed together with Algorithm

2.2 Packaging and shipment of clinical specimens

Specimens should be stored refrigerated until transported to the laboratory as soon as possible after collection. The specimens for diagnostic investigation should be packaged in accordance with the guidelines for the transport of dangerous biological goods in accordance with UN3373 Biological Substances/Category B shipping instructions (IATA packaging instruction 650). Specimens can be shipped on ice packs, but dry ice is not required.

2.3 Laboratory testing methods

Testing for the presence of MPXV should be performed in appropriately equipped laboratories by staff trained in the relevant technical and biosafety procedures (WHO, 2024).

The WHO does not recommend the use of rapid tests (lateral flow assays) (WHO, 2024)

2.3.1 Nucleic acid amplification testing and sequencing

It is recommended that mpox be investigated using nucleic acid amplification testing, using real-time or conventional polymerase chain reaction (PCR) on specimens (see Table 1) (WHO, 2024). Either mpox specific or Orthopoxvirus-generic assays may be used. No other orthopoxviruses are known to be present in South Africa. Nevertheless, where orthopoxvirus-generic assays are used, mpox-specific PCR, MPXV clade-specific PCR and/or sequencing must be performed to determine the species of virus involved. It is important to choose assays that may detect both Clade I and Clade II MPXV DNA. In accordance with WHO recommendations (WHO 2024), although sequencing of MPXV does not provide the same resolution to track chains of transmission as it does for RNA viruses (such as Ebola virus or SARS CoV2), a strategic and representative approach to sequencing of positive cases remains valuable for understanding the epidemiology of mpox in a country. Sequencing is however not required for diagnostic confirmation or to direct patient management decisions.

Targeted sequencing should be considered in specific situations, such as for atypical clinical presentations, imported cases, first cases in a newly affected geographic region, re-infections etc. Sequencing can assist with tracking of mutations that could lead to diagnostic failure if not recognized, suspected enhanced human-to-human transmission, or vaccine breakthrough cases, and to assess for antiviral resistance if needed in specific cases or situations.

A positive PCR result is confirmatory of the clinical diagnosis. A negative PCR finding should be carefully considered and if mpox is still considered the possible diagnosis, including in the presence of other diagnoses, testing on freshly collected samples may be requested on a case-by-case basis.

2.3.2 Electron microscopy and histology

Electron microscopy can be used to evaluate the specimen for poxviruses. Considering the availability of molecular assays and the high technical skills and facility required for this method, it is not routinely used for the diagnosis of poxviruses and cannot reliably distinguish between individual poxvirus species (although ortho-poxviruses could be distinguished from paradox viruses etc.). Histology may be informative for differential diagnosis of rash conditions but is not required for confirmation of mpox.

2.3.3 Viral culture

Virus isolation is not recommended as a routine diagnostic procedure and should only be performed in laboratories with appropriate experience and containment facilities and based on a risk assessment as required by the Hazardous Biological Agent Regulations, 2022 Also consider other requirements, for example registration with the Council for Non-Proliferation of Weapons of Mass Destruction as mpox virus is listed as controlled goods (see https://non-proliferation.thedtic.gov.za/)

2.3.4 Serology

Antibody detection from plasma or serum should not be used alone for clinical diagnosis of mpox. MPXV-specific antibody-based tests are expected to face challenges of cross-reactivity with antibodies to other ortho-poxviruses as well as those elicited by vaccination. The WHO recommends that serology testing should be restricted to reference laboratories until further evidence is available (WHO, 2024). Such testing may be useful for seroprevalence studies.

2.4 Access to laboratory testing in South Africa

Laboratory testing for mpox is available in the public and private health sectors of South Africa. Instructions for submission of specimens for testing from public sector facilities are available from the National Institute for Communicable Diseases (NICD) website (see https://www.nicd.ac.za/diseases-a-z-index/mpox-2/). The NICD serves as a national reference laboratory for mpox in South Africa*.

*** All private laboratories undertaking mpox testing must contact the NICD to ensure integration of data for reporting through the notifiable medical conditions (NMC) system and sequencing surveillance of mpox.**

3. CLINICAL MANAGEMENT OF MPOX

a. Mpox generally presents as a mild, self-limiting disease which resolves often without any medical intervention in two to four weeks. However, patients who are immunosuppressed or have comorbidities are at risk for more severe, and fatal, mpox. Pregnant woman and children are also at higher risk of presenting with severe disease.

Integrated Health Services: Offering HIV testing services alongside mpox treatments can improve overall health outcomes and individuals presenting with mpox symptoms should have the opportunity to be tested for HIV, as both infections can have serious health implications.

b. **Connection to care:** Early identification of HIV can facilitate timely linkage to care, which is essential to reducing morbidity and mortality. Those diagnosed with HIV can then receive antiretroviral therapy (ART), which significantly improves health outcomes and reduces the risk of transmission. If a patient has concurrent HIV infection and is on ART treatment, continue treatment. If not on ART treatment for HIV or defaulted, initiate ART on diagnosis or as soon as possible.

3.1 Management of mild or uncomplicated mpox

Patients with suspected or confirmed mpox with mild, uncomplicated disease and not at high risk for complications can be isolated at home, for the duration of the infectious period, as long as measures to limit spread to others can be employed at home. Considerations for mild or uncomplicated mpox:

- Ideally, a home assessment should be conducted when deciding to isolate and care for a person with suspected or confirmed mpox with mild uncomplicated disease in a home setting.
- A patient with mild, uncomplicated mpox cared for at home should be isolated in an area separate from other household members and away from shared areas of the home (that is, a separate room or area with a curtain or screen). Caution should be taken when handling and cleaning linens, household surfaces and during waste disposal.
- Symptomatic treatment such as antipyretics for fever and analgesia for pain should be considered. Conservative treatment of rash lesions should be performed dependent on their stage with aims to relieve discomfort, speed healing and prevent complications, such as secondary infections or exfoliation. Antibiotic therapy or prophylaxis is not warranted unless signs of secondary bacterial infection (i.e. cellulitis, abscess) are present.
- Patients with mpox should be assessed for their nutritional status and given adequate nutrition and appropriate rehydration.
- Counsel patients with mild mpox about signs and symptoms of complications that should prompt urgent care.

3.2 Management of severe mpox

3.2.1 Definition for severe mpox

Severe mpox disease is characterised by conditions such as:

- severe dehydration with or without shock
- haemorrhagic disease
- a large number of lesions such that they are confluent
- necrotic lesions
- severe lymphadenopathy that can be necrotising or obstructing (such as in airways
- involvement of multiple organ systems and associated comorbidities (for example, pulmonary involvement with nodular lesions; sepsis; encephalitis; myocarditis; ocular or periorbital infections); or other conditions requiring hospitalisation
- involvement of anatomic areas which might result in serious sequelae that include scarring or strictures these include lesions directly involving the pharynx causing dysphagia, inability to control secretions, or need for parenteral feeding
- lesions and severe oedema of the penile foreskin, vulva, vagina, urethra, or anorectum with the potential for causing strictures or requiring catheterisation
- anorectal lesions interfering with bowel movements (for example, severe pain); and severe infections (including secondary bacterial skin infections), especially those that require surgical intervention such as debridement.

3.2.2 Treatment for severe mpox 2

All patients should receive symptomatic and supportive treatment as outlined in this guide. Specific antiviral treatment for mpox should be considered for use in people with severe disease or who are at higher risk for severe disease:

- Patients who are severely immunocompromised due to conditions such as advanced or poorly controlled human immunodeficiency virus (HIV), leukaemia, lymphoma, generalised malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumour necrosis factor inhibitors, high-dose corticosteroids, being a recipient of a hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component.
- Paediatric populations, particularly patients younger than one year of age.
- Pregnant or breastfeeding women.
- People with a condition affecting skin integrity — conditions such as atopic dermatitis, eczema, burns, impetigo, VZV infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier’s disease (keratosis follicularis).

Table 3: Risk factors and clinical findings described as being associated with severe disease and poor outcomes (based on small, uncontrolled, observational studies).

Neurological symptoms	• New onset of confusion, seizures, or decreased level of consciousness may indicate severe involvement of central nervous system processes.
Vital signs	• Significant alterations in temperature, heart rate, respiratory rate, and blood pressure can indicate severe disease progression.
Delay in medical attention	• delayed seeking of medical care can result in worsened disease outcomes.
Gender	• In some diseases, male gender has been associated with worse outcomes.
Age	• Older adults are often at higher risk for severe disease due to weakened immune systems and comorbidities.
Comorbid conditions	• Chronic illnesses such as diabetes, hypertension, cardiovascular disease, chronic respiratory diseases, obesity, and immunocompromised states can increase the risk of severe disease.
Patient groups at higher risk of sever diseases or complications	• Children, pregnant women, persons who are immunosuppressed such as persons living with HIV having poorly controlled disease • Though data are lacking, patients with chronic skin conditions (that is, burns) may also be at higher risk for complications, such as bacterial infection
Clinical signs and symptoms of complications	• Nausea and vomiting, painful cervical lymphadenopathy causing dysphagia, poor oral intake, eye pain, vision abnormalities, hepatomegaly, sepsis, dehydration, respiratory distress/pneumonia, and/or confusion.
Laboratory abnormalities	• Elevated hepatic transaminases (AST and/or ALT), low blood urea nitrogen (BUN), low albumin, elevated white blood count (WBC), or low platelet count.
Skin lesion severity score	From smallpox experience -Mild (<25-99 lesions) -Moderate (25-99 skin lesions) -Severe (100-250 skin lesions) -Very severe (>250 skin lesions)

2 Call the NICD hotline, seek expert opinion to discuss patient for decision on Tecovirimat use
Source: WHO, Clinical management and infection prevention and control of monkeypox, Interim rapid response guidance 10 June 2022

For patients at high risk for progression to severe disease, treatment with Tecovirimat should be administered early in the course of illness along with supportive care and pain control. Brincidofovir and cidofovir have not been shown to be effective against MPXV infection in humans and are not recommended for treatment of severe mpox cases.

3.3 Special considerations

3.3.1 Immunocompromised patients including those living with HIV

Risk factors for severe mpox disease - Most patients, including those with well-controlled HIV, experience self-limiting disease and recover with supportive care alone. However, patients who are significantly immunocompromised, most commonly from advanced HIV (CD4 T lymphocyte [CD4] cell count <200 cells/mm^3 and especially <50 cells/mm^3), have experienced more severe infections, including increased likelihood of hospitalisation, disseminated disease and death. Although they may have a higher risk of infection and severe illness, severe outcomes are not universally seen in people who are immunocompromised.

Although, according to the HIV standard of care, ART initiation is delayed in some cases for IRIS concerns, clinicians should manage mpox in people living with HIV (PLWH) by ensuring timely access to antiretroviral treatment (ART), prioritizing vaccination, and providing supportive care for both conditions. Close monitoring for complications, including severe mpox or opportunistic infections, is crucial. Infection prevention and control measures, including isolation and contact tracing, should be implemented, particularly for PLWH with lower CD4 counts. Key Considerations for Clinicians:

- **Timely ART Initiation and Adherence**

Optimizing the immune system through ART is critical for clearing mpox infection, especially in PLWH with lower CD4 counts. Clinicians should ensure ART initiation, continuation, or resumption is prioritized in people who are co-infected with mpox and who are ART naïve or have had a prolonged interruption of ART. These patients should be referred to appropriate services for ART initiation, aiming to provide therapy within 7 days of diagnosis including offer of same day start.

- **Early testing**

Early HIV testing should be conducted when patients present with confirmed or presumptive mpox (see Appendix 9-12).

- **Prioritize Vaccination**

Mpox vaccination is recommended for PLWH, particularly those with lower CD4 counts, those who have been exposed or anticipate exposure, and those who are not yet on ART.

- **Supportive Care**

Manage mpox symptoms, such as pain and fever, and ensure adequate skin care. Consider antiviral medications like tecovirimat, especially in severe cases or for those at higher risk.

- **Monitoring for Complications**

PLWH are at increased risk for severe mpox and other opportunistic infections, including bacterial superinfections. Monitor for signs of severe disease, such as difficulty breathing or a deterioration in general condition and consider hospitalization if needed.

- **Infection Control**

Implement strict infection control measures, including isolation and contact tracing, to prevent transmission, especially in PLWH with lower CD4 counts who are more susceptible to severe disease. Follow local and national guidelines for isolation and quarantine.

- **Awareness and Counseling**

Educate PLWH about mpox, the importance of ART and vaccination, and how to reduce the risk of transmission, including avoiding close contact with infected individuals.

- **Collaboration with Specialists**

Collaborate with infectious disease specialists and HIV specialists to ensure comprehensive care for PLWH with mpox.

- **Address Stigma**

Recognize and address the stigma associated with both HIV and mpox to ensure PLWH receive appropriate care and support.

Specific Considerations for PLWH:

- **CD4 Count**

PLWH with lower CD4 counts (<200 cells/mm3, especially <100 cells/mm3) are at higher risk for severe mpox and should be monitored more closely.

- **Viral Load**

Controlling HIV viral load through ART is crucial for optimizing immune function and reducing the risk of severe mpox.
In people who are already on ART and with undetectable viral load, ART regimen should be continued without interruption or change.

- **Drug Interactions**

Be aware of potential drug interactions between ART and tecovirimat and ensure appropriate ART regimens are maintained.

- **Pre-Exposure Prophylaxis (PrEP)**

Continue PrEP in individuals already taking it and refer HIV-negative people with mpox to PrEP.

- **Sexual Health**

Advise on condom use and other barrier methods for sexual transmission and discuss the importance of reducing sexual partners and limiting venues where prolonged skin-to-skin contact is possible.

3.3.2 Women and persons who are pregnant or postpartum

In utero transmission of MPXV has been documented as has transmission from mother to child via direct contact. Cases of miscarriages or stillborn infants have been reported. The association between the severity of maternal illness and these outcomes is unclear. There are no data reported on the use of tecovirimat in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Tecovirimat is not recommended during pregnancy unless the benefits are considered to outweigh the risks. Pregnancy testing should be considered in individuals of childbearing potential to inform discussion about clinical risks and benefits.

3.3.3 Children

Tecovirimat is not recommended if under 13kgs, weigh risk and severity of symptoms.

3.3.4 Breastfeeding

WHO suggests that mothers with mpox continue breastfeeding, whilst limiting direct contact with their non-infected infant, until lesions are fully resolved (lesions are crusted, the scab of lesions have fallen off and a fresh layer of intact skin has formed underneath).
If breastfeeding is continued between a suspected or confirmed mother with mpox and a non-infected infant, IPC measures must be established including limited contact between mother and infant except during breastfeeding and coverage of active lesions on other parts of the body whilst breastfeeding.

The presence of areolar lesions should prompt careful consideration and mothers should not use that breast to breastfeed the infant. In the case of unilateral lesions, until lesions are healed (lesions are crusted, the scab of lesions have fallen off and a fresh layer of intact skin has formed underneath), breastfeeding may take place from the unaffected breast whilst covering all active lesions.

Healthcare workers should inform the mother about the risk of infection to infants whilst breastfeeding and availability of appropriate alternatives.

Context will drive the feasibility, availability and safety of alternatives to breast feeding. Whenever it is safe and feasible, expressed breastmilk or milk substitutes and no direct contact, may be pursued to reduce transmission.

While Tecovirimat is not indicated in breastfeeding, the risk of discontinuing breastfeeding should be discussed on an individual basis.

:

Contraindications

- Severe renal impairment
- Severe hepatic impairment
- Pregnancy

3.4 General management considerations

3.4.1 Clinical management of skin lesions

- Treatment of rash lesions depends on the stage of evolution of the rash.
- The aim is to relieve discomfort, speed healing and prevention of complications, such as secondary infections or exfoliation.
- The patient should be counselled not to scratch the skin. Patients should be instructed to keep skin lesions clean and dry to prevent bacterial infection. They should be instructed to wash hands with soap and water or use alcohol-based hand sanitiser before and after touching the skin rash to prevent infection. Then lesions may be cleaned gently with sterile water or antiseptic solution. The rash should not be covered but rather left to open air to dry.
- For complications of skin lesions such as exfoliation or suspicion of deeper soft tissue infection (pyomyositis, abscess, necrotising infection), consider consultation with appropriate specialist (that is, wound care specialist, infectious diseases specialist, and/or surgeon). Debridement of the skin should not be done unless performed by an expert wearing appropriate PPE. Optimal management of skin lesions is uncertain and needs further research.
- See section 3.1 for antibiotic treatment advice.
- •See appendix 11 for assessment and care of non-complicated and complicated mpox skin lesions.

3.4.2 Management of pain

In the public sector, pain is treated empirically and in line with the South African Standard Treatment Guidelines at the hospital level (https://www.health.gov.za/nhi-edp-stgs-eml/). Topical and systemic strategies should be used to manage pain. Pain management strategies should be individualised and patient-centred, tailored to the needs and context of an individual patient.
Managing pain is important when treating mpox patients because pain is a frequent and often severe symptom (for example, rectal pain, headache, muscle aches, pain from lesions, and lymphadenopathy pain). Pain management should be tailored to the individual patient, with a combination of non-pharmacologic and pharmacologic therapies as needed (refer to Appendix 12: pain management in patients with mpox).

Clinicians should assess the pain at the beginning and then regularly, and pain management should be adjusted as required. Mild pain can be treated with medications such as acetaminophen or ibuprofen, while short-term management of severe pain (for example, severe rectal pain due to proctitis) may require opioids such as tramadol or morphine, after assessing the benefits and risks of opioid use. Rinsing with salt water at least four times a day may help patients who have rash inside the mouth. Additionally, local anaesthetics (for example, viscous lidocaine) or prescription mouthwashes can be recommended to relieve the pain. Starting treatment with tecovirimat early on may help alleviate pain in patients with severe proctitis, but more evidence is needed. For systematic pain management tailored to mpox cases (please refer to Appendix 12).

3.4.3 Proctitis

Rectal pain is a common complication of mpox, and proctitis has been frequently reported. Complications of rectal involvement have included rectal perforation and perianal abscess.

Stool softeners should be considered for patients with proctitis to reduce pain associated with bowel movements. Oral acetaminophen or NSAIDs can provide symptomatic relief. Topical anaesthetics (e.g., topical lidocaine) may offer symptomatic relief. Pain from proctitis may be severe and may require prescription medications or sometimes require hospitalization for pain management. Adjunctive pain relief with neuropathic pain agents, such as gabapentin may provide relief of proctitis symptoms based on anecdotal reports to date. In the public sector, Gabapentin is available at tertiary level for patients with peripheral neuropathy refractory or intolerant to standard of care (e.g. amitriptyline; or carbamazepine).

Warm sitz baths (warm bath made up of water and baking soda or Epsom salt) could be considered for symptomatic relief. While autoinoculation or person-to-person transmission of mpox virus has not been associated with sitz baths, we recommend that sitz baths be drained and disinfected immediately after use.

Secondary bacterial infections have been reported and should be considered if there are progressive symptoms such as erythema, pain, or swelling, which may indicate abscess formation.

3.4.4 Oropharyngeal lesions

Severe oropharyngeal manifestations of mpox virus infection have been reported, including tonsillar edema, peritonsillar abscess, and epiglottitis. Such symptoms may limit the ability to tolerate oral therapy and maintain hydration and caloric intake.
For management of oropharyngeal symptoms, patients can **consider rinsing** the mouth with clean saltwater four times a day. **Oral antiseptic** (e.g., chlorhexidine mouthwash), local anaesthetic (e.g., viscous lidocaine), and prescription analgesic mouthwash (sometimes called "magic mouthwash") can also be considered if available. There are different potential ingredients (e.g., antihistamine, anaesthetic) for prescription analgesic mouthwash; healthcare professionals can work with pharmacists to identify the optimal ingredients for their patients.

3.4.5 Ocular manifestations

The virus may enter the eye via autoinoculation and cause a range of problems from mild to severe, including conjunctivitis, blepharitis, keratitis, and corneal ulcer, corneal scarring, and rarely loss of vision. Corneal scarring and vision loss are potential severe consequences of ocular involvement. Bacterial superinfection of corneal ulcerations can cause severe complications. The constellation of facial and ocular symptoms was observed in association with systemic symptoms (for example, fever, painful cervical adenopathy) and risk factors for sexual transmission.

If ocular involvement is suspected, then ophthalmologic consultation should be strongly considered for a thorough evaluation and continued monitoring of the patient's condition and extent of disease, especially in cases of vision changes, eye pain, or increasing redness. Acute infection can currently be diagnosed by PCR testing of swabs of lesions on the conjunctiva in already confirmed mpox cases. Clinical judgment should be used in assessing the stability of underlying eye structures, and caution should be taken with obtaining swabs if corneal ulcers or severely painful lesions are present.

Slit lamp examination and dilated funduscopic examination can help determine whether anterior segment structures (conjunctiva, cornea, iris) or posterior segment structures (retina, nerve, choroid) are involved. Infection prevention and control precautions and equipment disinfection protocols are recommended when examining patients at the slit lamp biomicroscope. **Trifluridine may be considered** (where available) in cases of mpox conjunctivitis and is recommended in cases of mpox keratitis, in consultation with an ophthalmologist. Trifluridine is a topical antiviral used for the management of herpes-simplex keratitis. Additionally, patients with corneal disease, including corneal ulcer, consider topical lubricants and/or antibiotics to prevent bacterial superinfection, which can be a vision-threatening complication of corneal ulcer.

3.4.6 Mental healthcare

In the context of mental healthcare, particularly when dealing with complexities such as home isolation due to conditions like mpox, referrals to appropriate mental health professionals and support services are critical. Here are some considerations based on the query: **Mental Health Act Context: Chapter 2 of the Mental Health Act (Act 17 of 2002)** emphasizes the importance of promoting mental wellbeing and recognising the role of social care in maintaining mental health. For individuals experiencing milder anxiety or depressive symptoms, especially those in home isolation, social workers can provide crucial support. They can assist with:

- Social needs assessment and resources such as food and healthcare access.
- Emotional support and counselling.

Coping strategies for managing stress and anxiety due to isolation
A diagnosis of mpox can lead to significant mental and psychosocial effects, including fear of the disease or death; loss of sense of the meaning of life; or loss of faith; physical and social

isolation from family or community; stigma associated with diagnosis and returning to the community, scarring and disability (for example, blindness) associated with the disease. Patients with mpox should receive compassionate, respectful, people-centred care consistently while ensuring appropriate and adequate protection of household members, visitors and health workers. Basic psychosocial support skills are essential for management of all patients and represent an integral part of the care that should be provided for all.

3.4.7 Tecovirimat

Tecovirimat is an oral agent originally developed for the treatment of smallpox. Activity against MPXV has been shown in non-human primates. It is an inhibitor of the orthopoxvirus VP37 envelope wrapping protein and is indicated for the treatment of human smallpox disease in adults and paediatric patients weighing at least 13 kilograms (kg). Studies have shown good safety data when evaluated in humans but randomized controlled trials of safety and efficacy in humans with mpox diseases were lacking. The recent PALM007 study in the Democratic Republic of Congo showed that tecovirimat did not reduce the number of days to lesion resolution in children and adult patients with disease caused by clade 1 MPXV. Improvement in clinical status of patients was rather due to a package of care with attention to improving the nutritional status in paediatric patients. The STOMP study conducted in adults with mild to moderate MPXV clade 2 did not show efficacy in time to skin and mucosal skin resolution. Results of further studies in different population groups with severe disease are awaited.

In the interim tecovirimat may still be considered for treatment of severe MPXV infections and used according to national and international guidelines. Given the limited evidence related to use of tecovirimat at the moment (pending results of the RCT), NEMLC suggest that only those hospitalised with severe mpox should be considered for treatment. The efficacy of tecovirimat may be reduced in immunocompromised patients.

Tecovirimat is indicated for selected patients with PCR-confirmed mpox who have acute illness compatible with current mpox infection plus any of the following: primary /secondary immunodeficiency; extensive lesions (>100); complications – ocular, CNS, complex lesions in urogenital tract that interfere with urination, lesions that interfere with swallowing/breathing. intractable pain.

Dosage: SIGA-Tpoxx®. PO (600mg bd x 14 days), crush if necessary; longer course in immune suppressed. The drug is well tolerated; minor adverse effects include dry mouth, mild nausea and diarrhoea. Dysphoria has been reported.An intravenous formulation is available in some countries.

All persons with confirmed MPXV infection should be tested for HIV, and antiretrovirals should be initiated as soon as possible in those not on treatment. More severe MPXV infections are well noted in those PLHIV not on ARV therapy. IRIS has not been a usual occurrence.

INdications for tecovirimat

Hospitalised patients must meet the eligibility criteria but none of the exclusion criteria listed below:

- MPXV infection is confirmed by polymerase chain reaction (PCR) testing

AND

- symptomatic with a syndrome compatible with ongoing MPXV infection

AND

- meeting any one or more of the criteria for severe or complicated disease as outlined below:
- critical illness where MPXV infection is considered to be a key factor driving the critical condition of the patient
- intractable pain
- **Non-opioid analgesics:** Paracetamol (acetaminophen), non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, diclofenac, and aspirin. Defined as patients who have been prescribed topical and systemic analgesia using World Health Organization (WHO) pain ladder with at least 24 hours exposure to opioids (if clinically appropriate)
- rectal abscess or fistula formation
- upper respiratory tract mucocutaneous involvement that is affecting swallowing or airways
- patient with primary or acquired immunodeficiency, or on immunosuppressive medication as per HIV management guideline.
- extensive cutaneous disease (for example more than 100 lesions or a large number of lesions such that they are confluent or necrotic).
- haemorrhagic disease.
- severe lymphadenopathy that can be necrotising or obstructing (such as in the airways, or urinary tract).
- involvement of multiple organ systems and associated comorbidities (for example, pulmonary involvement with nodular lesions; sepsis; encephalitis; meningitis or other neurological manifestation, myocarditis; ocular or periorbital infections); or other conditions requiring hospitalisation.
- involvement of anatomic areas which might result in serious sequelae that include scarring or strictures — these include lesions directly involving the pharynx causing dysphagia, inability to control secretions, or need for parenteral feeding.
- lesions and severe oedema of the penile foreskin, vulva, vagina, urethra, or anorectum with the potential for causing strictures or requiring catheterisation.
- anorectal lesions interfering with bowel movements (for example, severe pain); and severe infections (including secondary bacterial skin infections), especially those that require surgical intervention such as debridement

Exclusion criteria

Patients are not eligible for treatment if any of the following apply:

- Hospitalised for reasons other than monkeypox virus infection or do not meet any of the criteria for severe and complicated disease
- Known hypersensitivity reaction to the active substances or to any of the excipients of the medications below as listed in their respective SPC.

Relative contraindication

There is a lack of sufficient evidence to inform guidance on use of tecovirimat in children of less than 13 kg body weight. Weigh risk and severity of symptoms and seek expert opinion if weight is less than 13kgs.

Tecovirimat is not a registered drug in South Africa. The use of the drug is authorised through Section 21 Access to Unregistered Medicines application with the South African Health

Products Authority. Tecovirimat is available as an oral capsule (200 mg) and injection for intravenous (IV) administration. IV Tecovirimat is not available in South Africa. Refer to Table 4 for oral administration:

Table 4: Proposed weight-based oral dosing and drug food preparation instructions for patients who cannot swallow capsules.

Body weight in kgs	Dose (mg)	Number of capsules	Frequency	Route	Instructions for patients who cannot swallow
120 and above	600	3 capsules	Three times a day every eight hours	Oral	Mix contents of 3 capsules with 30 ml. of liquid or soft food.
40 to less than 120	600	3 capsules	Twice per day every twelve hours	Oral	Mix contents of 3 capsules with 30 ml. of liquid or soft food.
25 to less than 40	400	2 capsules	Twice per day every twelve hours	Oral	Mix contents of 2 capsules with 30 ml. of liquid or soft food.
13 to less than 25	200	1 capsule	Twice per day every twelve hours	Oral	Mix contents of 1 capsules with 30 ml. of liquid or soft food.
6 to less than 13	100	½ capsule	Twice per day every twelve hours	Oral/ Nasogastric tube	Mix contents of 1 capsule with 30 mL[1] of liquid or soft food. Administer one half of mixture (15 mL) to patient. Discard unused mixture
Less than 6	50	¼ capsule	Twice per day every twelve hours	Oral/ Nasogastric tube	Mix contents of 1 capsule with 30 mL5 of liquid or soft food. Administer one quarter of mixture (7.5 mL) to patient. Discard unused mixture.

For participants who cannot swallow capsules, study drug can be prepared by carefully mixing the required contents in 30ml. of liquid (e.g., milk, chocolate milk) or soft food (e.g., apple, sauce, yoghurt). The entire mixture should be administered within 30 minutes of its preparation.

- Treatment duration: 14 days, but may be longer (not to exceed 90 days) or shorter depending on disease progression and patient's clinical condition[1]
- Dosing should be taken with food.

Note:
Adverse reactions may include headache (12%); nausea (5%); abdominal pain (2%); vomiting (2%). Drug interactions have been reported in healthy adults with co-administration of repaglinide (hypoglycaemia) and midazolam (decreased effectiveness of midazolam).

Mpox Discharge Criteria
Patients with mpox are considered to pose no further risk of transmission once all symptoms have resolved and the vesicular lesion scabs have completely separated, which typically occurs after a minimum of 21 days.

The virus can persist in body fluids and potentially be transmitted through direct contact with infected individuals or contaminated fomites. Immunocompromised individuals, particularly those with HIV and low CD4 counts, are at higher risk of severe disease and prolonged viral shedding, necessitating stringent isolation until full recovery.

The presence of viremia during symptomatic infection, which can last 2-3 weeks post-rash resolution, underscores the importance of ensuring complete recovery before considering the patient non-infectious.

Education and awareness, particularly among high-risk groups such as men who have sex with men (MSM) and people living with HIV/AIDS (PLWHA), are essential to prevent further spread and ensure timely diagnosis and treatment.
Therefore, consider discharge when ALL 3 criteria below are met.
1. Clinical improvement and resolution of ALL non-skin symptoms (no fever, severe respiratory distress, or complications like secondary infections (Stable vital signs RR, B/P, HR/ SPO2 within normal for 48 hours).

AND
2. All lesions have re-epithelialized, and no new lesions have appeared over the past 48 hours. This applies to ALL lesions including skin and mucosal lesions such as mouth, vagina etc.

AND
3. The patient can eat, drink, and manage personal hygiene independently or with minimal assistance.
If having sex, use condoms as a precaution for 12 weeks (about 3 months) after you have recovered

[3] In laboratory experiments, consistent suspension was not attained in the lowest doses. Thus, administration of the 50mg and 100mg dosing is recommend via nasogastric tube
[4] Liquid/soft food volume as noted as per physician/pharmacy discretion
[5] Patients with severe disease may require longer duration of treatment, speak to the NICD clinician hotline

3.4.8 Infection prevention and control

If the person with mpox is an acute infection patient or is at risk of complications, they should be managed in a health facility setting and have more supportive care. Only mild, non-complicated cases of mpox should be managed with home-based care.

Infection prevention and control (IPC) measures for suspected and confirmed mpox cases are provided in the IPC Standard Operating Procedure for Healthcare Management of mpox Patients (National Department of Health, South Africa).

Infection prevention and control (IPC) practices for managing cases of mpox are essential to mitigate transmission and protect public health. The approach in South Africa, as in many other countries, involves several key strategies. Below is a summary of infection prevention and control practices specific to mpox cases:

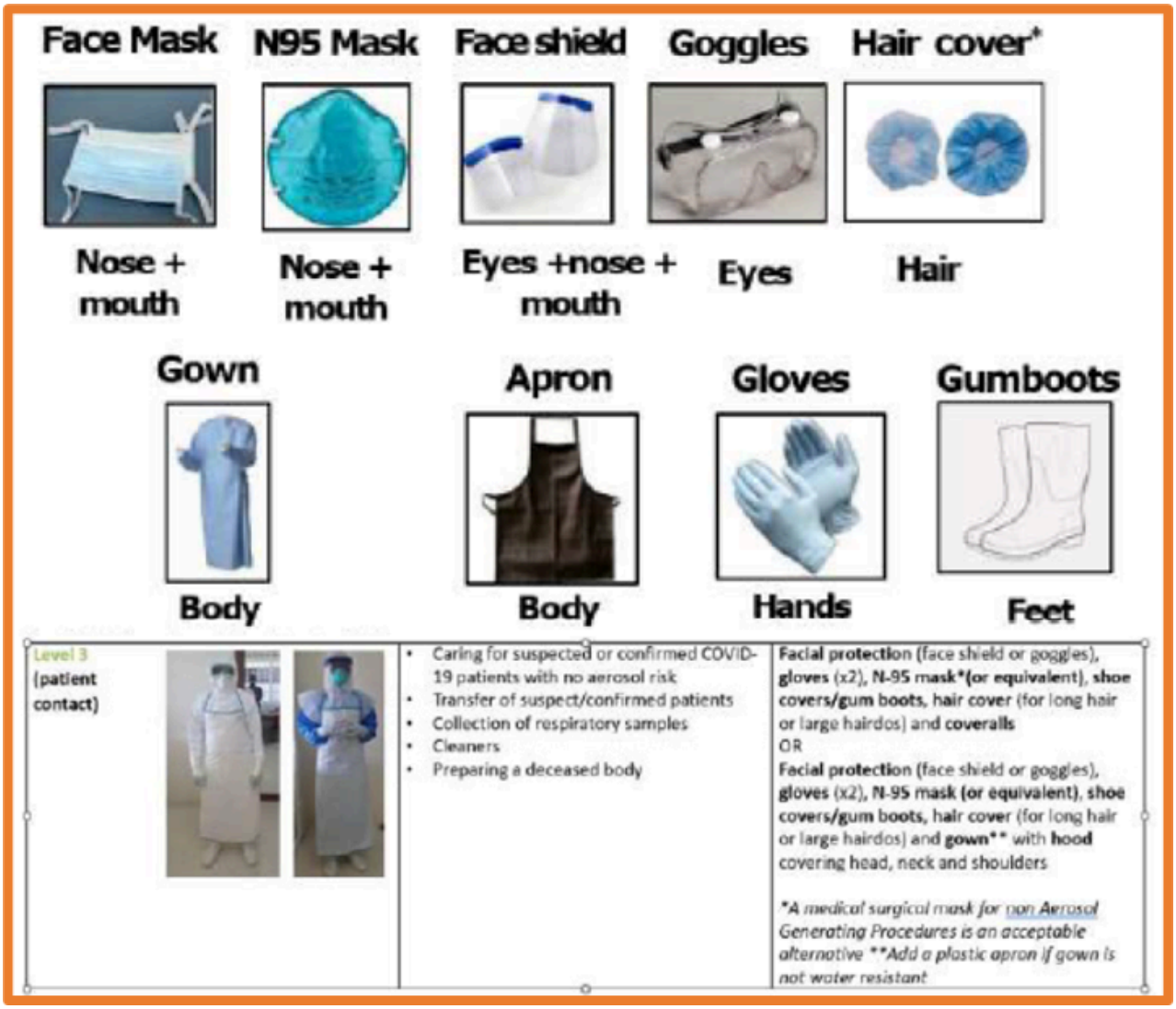
Isolation and Quarantine:

- **Isolation of Cases:** Confirmed cases should be isolated from non-infected individuals to prevent transmission, ideally in a healthcare setting that follows strict IPC protocols.
- **Quarantine of Contacts:** Individuals who have been in close contact with confirmed cases may need to be quarantined for monitoring symptoms.

Personal Protective Equipment (PPE):

- **Use of PPE:** Healthcare workers and caregivers should wear appropriate PPE, including gloves, masks, gowns, and eye protection when caring for infected patients or handling contaminated materials. In patients with suspected or confirmed mpox infection, WHO suggests that health and care workers use contact and droplet precautions.
- **Hand hygiene:** Infection prevention and control measures including hand hygiene, dedicated personal items, appropriate handling of linens and laundry, cleaning and disinfection of the environment, and waste management should be followed for persons with mpox in the community until all lesions are healed (lesions have crusted, scabs have fallen off and a fresh layer of skin has formed underneath).
- **Training on PPE Use:** Regular training on proper donning and doffing techniques for PPE to minimise contamination risks

PPE Components for Mpox



Hygiene and Sanitation:

- **Hand Hygiene:** Frequent handwashing with soap and water or using alcohol-based hand sanitisers, especially after contact with patients or contaminated surfaces.
- **Cleaning and Disinfection:** Regular cleaning and disinfection of surfaces and equipment in healthcare settings, particularly in areas where infected patients are managed.

Safe Handling of Biological Materials:

- •Guidelines are available for the safe handling, transport, and disposal of laboratory specimens to prevent exposure to potentially infectious materials. See https://www.nicd.ac.za/wp-content/uploads/2020/11/NICD-Laboratory-Handbook_V18.pdf

IPC Considerations in the Community

Patients who are in the community, prior to transfer to a facility should be isolated in an area separate from other household members and away from shared areas of the home (i.e. a separate room, or area with a curtain or screen).

Key issues:

- Designate one person to facilitate care of the patient
- The patient with Mpox should stay in a dedicated, well-ventilated room (e.g., with windows that can be opened frequently) separate from others in the household.
- Household members and patients with Mpox should clean their hands with soap and water or an alcohol-based hand sanitizer frequently. In addition, household members should avoid entering the room.
- If the designated person that is facilitating self-care needs to enter the isolation area, they should maintain a distance of at least 1 meter from the patient. When distance cannot be maintained, the designated person is to wear a well-fitting medical mask and disposable gloves. They should practice standard precautions at all times.

Caution should be taken when handling and cleaning linen, and household surfaces and during waste disposal.

Public Awareness and Education:

- **Community Education:** Initiatives aimed at educating the community about mpox, its transmission, and prevention measures, including avoiding contact with infected animals and reducing close contact with infected individuals.
- **Stigma Reduction:** Addressing stigma associated with mpox to encourage individuals to seek care without fear of discrimination.

3.4.9 Vaccination

- **Pre-exposure vaccination of high-risk group:** Vaccination should be offered in a staggered approach targeting GBMSM and transgender people at highest risk of exposure in districts with reported cases. Those considered at the highest risk are people with a recent history of multiple sex partners and those participating in group sex including health workers in frontline patient care (mpox cases) and laboratory workers performing mpox testing.
- **Post-Exposure Prophylaxis (PEP):** Consideration of vaccination for individuals who have been in close contact with confirmed cases, if available; smallpox vaccines may provide cross-protection against mpox according to the National Advisory Group on Immunisation (NAGI).

Travel and Immigration Measures:

- •Guidelines on travel restrictions or health screenings for individuals coming from areas with reported mpox outbreaks is available on https://www.nicd.ac.za/mpox-updates

Coordination with Health Authorities:

Collaboration: Working with local and national public health authorities to ensure a cohesive response to mpox, including data sharing and coordinated efforts for managing outbreaks.

APPENDICES

In the public sector, mpox cases are managed at tertiary level with support from expert clinicians in accordance with the Standard Treatment Guidelines (STGs). Refer to the STGs: https://www.health.gov.za/nhi-edp-stgs-eml/

Appendix 1: General guidelines for taking a sexual history

Herewith a guideline for taking sensitive but accurate sexual history from a patient (Savoy et al. 2020, Sexual health history: techniques and tips. Am Fam Physician. 2020;101(5):286-293)

Key points to ensure a productive sexual health conversation:

- Avoid moral or religious judgment of the patient's behaviour
- Avoid terms that make assumptions about sexual behaviour or orientation and ensure shared understanding around terminology and pronunciation for patient concerns to avoid confusion
- Establish rapport and consent before addressing sensitive issues
- Use a sensitive tone and use neutral and inclusive terms that avoids assumptions
- Respect the patient's privacy and be culturally sensitive and use gender inclusive language
- Create a safe space for the conversation

Gender inclusive terminology:

Sex: Determination made at birth referring to biological category of male, female, intersex
Sexual orientation: Self-determined sexual identity in relation to genders that one is emotionally, romantically, or sexually attracted to
Cisgender: Self-determined term when gender is aligned with sex (assigned at birth)
Transgender: Self-determined term when gender is not aligned with sex (assigned at birth)
Gender identity: Self-determined sense of being along (female, male, combination of both or somewhere in between) or outside of a gender spectrum resulting from multiple factors such as biological characteristics, environmental and cultural factors, and self-understanding
Gender expression: Signals or external ways that a person expresses their gender identity
Gender perception: The way others interpret a person's gender

Questions for a detailed sexual history using the 5P model:

General questions: Are you currently sexually active? Have you ever been sexually active? What is your gender? How do you identify? What pronouns do you prefer?

- **P**artners: How do your partner/s identify? How many partners have you had in the past month? The past six months? Lifetime?
- **P**ractices: What sexual activities do you partake in? Do you participate in vaginal sex? Oral sex? Anal sex?
- **P**ast history/protection: Have you ever had any sex-related infectious diseases? Have you ever been tested for HIV? Would you like to be tested for HIV? What do you do to protect yourself from HIV and other sex-related diseases?
- **P**regnancy plans: Are you trying to conceive a baby (if not pregnant)? What method of contraception do you use?
- **P**leasure: Do you use any devices to enhance pleasure during sex? Do you share the devices with others?

Appendix 2: Mpox screening tool for healthcare facilities

Version1 (09.08.2024) **Primary screening (at the entrance to health facility, by trained Health worker)**



SEXUALLY TRANSMITTED INFECTIONS (STIs)/M-POX/HIV SCREENING TOOL

Clinic Name: _____

Patient Name: _____ **Patient File Number:** _____

Age: _____ **Sex:** _____

SUSPECTED CASE DEFINITION

- ☐ This form must be used for screening in key population clinics AND/OR individuals that meet the suspected case definition for Mpox.
- ☐ Start with Section 1.

1. **Section 1: Contact Screening:**

Contact	Present (Yes/No)	If yes, date of contact
Has the patient had contact with a probable or confirmed Mpox case in the past 21 days?		

Complete Sections 2.1 and 2.2.

2. **Section 2.1: Symptom screening:**

Symptoms	Present (Yes/ No)		If yes, date of onset
Unexplained acute rash within the past 7 days and any one of the following	Yes ☐	No ☐	
Fever >38.5C* in the past 7 days	Yes ☐	No ☐	
Headache*	Yes ☐	No ☐	
Asthenia (profound weakness) *	Yes ☐	No ☐	
Muscle pain (myalgia)*	Yes ☐	No ☐	
Fatigue*	Yes ☐	No ☐	
Sore Throat*	Yes ☐	No ☐	
Generalized lymphadenopathy*	Yes ☐	No ☐	
Chills or sweats*	Yes ☐	No ☐	
Conjunctivitis*	Yes ☐	No ☐	
Back pain*	Yes ☐	No ☐	
2. Other STI and Mpox symptoms			
Genital discharge†*	Yes ☐	No ☐	
Skin rash/blisters/ulcers (face, chest, back, hands feet) ‡*	Yes ☐	No ☐	
Genital ulcers, blisters †*	Yes ☐	No ☐	
Anogenital pain and/or bleeding*	Yes ☐	No ☐	
Oral skin/mucosal lesions‡*	Yes ☐	No ☐	
NOTES:			

1

Appendix 3: Section 21 Tecovirimat access process

1.Patient suspected mpox: Initial suspicion based on symptoms.
2.Patient PCR confirmed mpox: Confirmation of mpox via PCR test.
3.Patient hospitalised and met case definition of severe infection: Criteria for hospitalisation based on severity, and recommendation from NICD clinical team to use Tecovirimat.
4.Submit per patient Section 21 application to SAHPRA: Application submission for each patient to the South African Health Products Regulatory Authority (SAHPRA), use online application portal ensure per patient tab is used.
5.Email application reference number to **Pharmaceutical Policy Epidemiology Specialist** within the **Directorate: Child and Youth Health** at the **National Department of Health** who will fast track application approval with SAHPRA
6.SAHPRA approval granted: Authorisation received from SAHPRA email approval to the **Pharmaceutical Policy Epidemiology Specialist** within the **Directorate: Child and Youth Health** at the **National Department of Health**
7.Tecovirimat capsules issued by bulk storage site: Medication issued in line with SAHPRA approval.
8.Public or private sector institution arrange collection of capsules in Pretoria: Coordination for collection by the treating institution, **Pharmaceutical Policy Epidemiology Specialist** within the **Directorate: Child and Youth Health** at the **National Department of Health** will provide the details of the pharmacy where the stock should be collected.
9.Tecovirimat issued to patient by treating institution: Distribution to the patient, treating institution to dispense in line with prescription.
10. Treating physician to report on progress and ADR to SAHPRA as per patient Sec 21 approval.
11. Treating physician to complete WHO reporting tool through the WHO Global Clinical Platform (https://www.who.int/tools/global-clinicalplatform/monkeypox), which shall include reporting of: (i) all anonymized patient data, including clinical information (concurrent conditions, symptoms), (ii) all clinical outcomes, and (iii) any complications experienced during the course of hospitalisation or course of treatment.
12. Any suspected unexpected serious adverse reactions (SUSARs) that are life-threatening and any other potentially treatment related serious adverse events (SAEs) are promptly reported to the national pharmacovigilance centre, WHO and SIGA. For WHO, such SUSARs and SAEs will be reported as follows: by mail addressed to World Health Organization, Regulation and Prequalification Department, 20 Avenue Appia, 1211 Geneva 27, Switzerland, and via email at pvsupport@who.int.

Appendix 4: Vital signs and clinical features to monitor systematically.

Vital signs and pain assessment	• Temperature, heart rate, blood pressure, respiratory rate, peripheral oxygen saturation, level of consciousness using the alter, voice, pain, unresponsive scale (AVPU), point of care glucose, and body weight and height to calculate BMI and children's mid-upper arm circumference (MUAC). • Pain scale.
General condition	• Is the patient able to eat and drink without support? • Is the patient able to sit and walk independently? • Has the patient had recent weight loss since onset of symptoms?
Rash characterisation	• Stage of rash: macules, papules, vesicles, pustules, crusted over, exfoliation. • Location of the rash (face, arms, torso, genitals, legs, mucosa) • Number of lesions • -Mild (<12 skin lesions) • -Moderate (25-99 skin lesions) • -Severe (100-250 skin lesions) • -Very severe (>250 skin lesions) • If exfoliation present: %body affected (>10% is concerning)
Presence of bacterial secondary infection	Cellulitis, abscess, pyomyositis, necrotising soft tissue infection
Neurological status	AVPU, seizures, coma
Volume status	Presence of dehydration: mild, moderate, or severe
Signs of perfusion	Pulse rate, strength, capillary refill Urine output (>0.5mL/kg/hr=good in adults; 1.0mL/kh/hr in children) Mottling of skin
Respiratory system	Respiratory rate, Sp02, signs of respiratory distress
Nutritional assessment	Change in appetite, weight loss, body weight, height, calculation of BMI, MUAC in children Signs of malnutrition-use standardised tool (e.g. Malnutrition Universal Screening Tool)
Laboratory tests	Na, K, HCo, BUN, creatinine, AST, ALT, glucose, white blood count, Hg, platelet, PT/INR, Cl, calcium, albumin

Source: WHO, Clinical management and infection prevention and control of monkeypox, Interim rapid response guidance 10 June 2022

Mpox can clinically resemble various rash illnesses which need to be considered during differential diagnosis. Below are some examples:

- Varicella zoster virus (VZV, chickenpox)
- Measles
- Chickenpox
- Scabies
- Skin and other soft tissue infections
- Medication associated allergies
- Molluscum Contagiosum
- Pruritic urticarial papules and plaques of pregnancy
- herpes simplex virus (HSV),
- primary or secondary syphilis,
- disseminated gonococcal infection
- foot and mouth disease,
- chancroid,

Appendix 5: Clinical management of complications and severe forms of mpox

Complication	Treatment
Skin Exfoliation	Heavy rash burden can lead to exfoliation (similar to partial thickness burns), dehydration, and protein loss. Estimate percentage of skin affected; treat like burns. Minimise fluid loss and promote skin healing. Ensure adequate hydration and nutrition. Consult surgeon, dermatologist, or wound care specialist. Debridement and skin grafting if needed.
Necrotising Soft Tissue Infection	Life-threatening deep tissue infection with necrosis and systemic toxicity. Suspect with oedema, crepitus, malodorous discharge, or severe pain. Consider bacterial causes; start broad-spectrum antibiotics. Consult surgeon for surgical emergency.
Pyomyositis	Suspect when muscle tenderness occurs; can be caused by MPX or skin flora like Staphylococcus or Streptococcus. Use ultrasound for diagnosis, collect blood cultures, start broad-spectrum antibiotics, and perform surgical drainage.
Cervical Adenopathy	Can occur in 85.65 per cent of cases with lymphadenopathy. Large adenopathy with oropharyngeal lesions may risk respiratory compromise and dehydration. Consult surgeon, anaesthesiologist, and infectious disease specialists; steroids may be used in severe cases.
Ocular Lesions	Risk of corneal scarring and vision loss; may present as conjunctivitis. Immediate ophthalmologist evaluation. Use ophthalmic antibiotics/antivirals, vitamin A, eye lubrication, and saline-soaked protective pads. Avoid steroid ointments; consider trifluridine eye drops if indicated.
Pneumonia	Follow WHO guidelines for severe acute respiratory infections. Provide supportive care and oxygen therapy. Administer antibiotics if bacterial superinfection is suspected.
Acute Respiratory Distress Syndrome (ARDS)	Provide oxygen, non-invasive ventilation, or mechanical ventilation as needed. Manage according to the WHO guidelines for severe acute respiratory infections.
Severe Dehydration	Caused by intravascular volume loss due to rash or gastrointestinal symptoms. Resuscitate with IV or IO fluids, monitor closely. Follow WHO guidelines for children if applicable.
Sepsis and Septic Shock	Caused by immune response to infection. Early identification and infection management with supportive care, fluid resuscitation, and vasopressors if needed. Follow WHO guidelines for severe acute respiratory infections.
Encephalitis	Consider lumbar puncture for CSF evaluation. Monitor and support ABCD (airway, breathing, circulation, disability). Control seizures, administer antibiotics/antivirals if indicated.
Nutritional Considerations	Assess nutritional status; assist feeding if needed. Consider enteral nutrition if oral intake is insufficient. Monitor patients at risk for refeeding syndrome and start enteral feeding slowly. Do not force-feed patients with reduced consciousness; refer to WHO guidelines for severe malnutrition.

Source: WHO, Clinical management and infection prevention and control of monkeypox, Interim rapid response guidance 10 June 2022

Appendix 6: Mpox screening tool for health workers

Mpox screening tool for health workers

Characteristic mpox acute skin rash

- Single or multiple lesions in any part the body and/or mucosa that may include oral, conjunctival, urethral, penile, vaginal or anorectal lesions (anorectal lesions can manifest as anorectal inflammation [proctitis], pain and/or bleeding).

Characteristic mpox lesions

- Sequential stages: macules, papules, vesicles, pustules, crusting over and desquamative lesions over a period of 2–3 weeks.
- Typically, all lesions are at same stage and start centrally, extending towards palms of hands and soles of feet.
- Lesions can range from one to a few and, in severe cases, even several thousand.
- Can involve mouth, genitals and eyes.

YES

Enter mpox pathway
- IPC precautions for mpox
- Triage and clinical assessment

NO

Seek usual care



Source: Bichat Claude Bernard Hospital, APHP (France)



Source: Lagos State University Teaching Hospital (Nigeria)



Source: Evandro Chagas National Institute of Infectious Diseases-Fiocruz (Brazil)



Source: Hospital Clinic de Barcelona (Spain)



Source: Evandro Chagas National Institute of Infectious Diseases-Fiocruz (Brazil)



Source: University of Toronto (Canada)



Source: Hospital Clinic de Barcelona (Spain)



Source: WHO photo library



Source: Evandro Chagas National Institute of Infectious Diseases-Fiocruz (Brazil)



Source: Hospital Clinic de Barcelona (Spain)

See Atlas of mpox lesions: a tool for clinical researchers, 28 April 2023, version 1.0. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/366569).

World Health Organization

Appendix 7: Mpox triage and clinical assessment for suspected and confirmed cases

Mpox triage and clinical assessment for suspected and confirmed cases

Each suspected case should have a clinical assessment of severity and risk factors before deciding to admit to the health facility or refer for home care. This decision should be made on a case by case basis by clinical staff.

A B C D E assessment[1]



A
Airway: check patient for signs of obstruction, noises



B
Breathing: respiratory rate, depth, accessory muscles, nasal flaring, symmetry, SpO_2



C
Circulation: Pulse, blood pressure, CRT, urine output



D
Disability: AVPU, blood glucose, seizures



E
Exposure and history taking

What are the signs or symptoms of complication of mpox?

1. **Fever:** uncontrolled or persistent fever.
2. **Pain:** uncontrolled or persistent pain.
3. **Skin secondary infection:** extreme redness, tenderness, pus or further disseminated mpox lesions.
4. **Mucosa affected:** extensive mucosal lesions (rectal, genital, oral) impeding function, e.g. trouble swallowing, pain with urination or defecation.
5. **Nausea and/or vomiting:** uncontrolled or persistent.
6. **Limited oral intake:** dehydration and signs of malnutrition.
7. **Trouble breathing:** fast respiratory rate.
8. **Swelling neck:** difficulty swallowing or breathing.
9. **Shock:** weak pulse, bad perfusion, reduced urinary output, tachypnea, altered mental status, hypotension.
10. **Eye:** altered vision, painful or red eye.
11. **Co-morbidities** decompensated including lung, kidney, heart, liver, skin, metabolic, mental health or sickle cell disease.

YES

- Admit to the health facility mpox isolation ward.
- Provide symptomatic treatment including for pain, nutrition, skin and eye care if required.
- Provide optimized supportive care treatment.

NO

- Preferred Isolation in a health facility and early care of complications.
- If not possible, home care can be considered if the appropriate criteria are met.[2]

High risk populations for severe disease:

- Children less than 5 years of age.
- Pregnant women.
- Immunosuppressed persons such as those living with HIV (particularly CD4 < 200)[3].

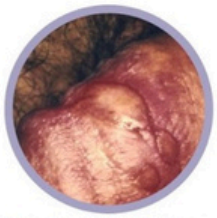
[1] Basic emergency care. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/275635).
[2] Infection prevention and control and water, sanitation and hygiene measures for home care and isolation for mpox in resource-limited settings: interim operational guide. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/379477).
[3] Consolidated guidelines on HIV testing services. Geneva: World Health Organization; 2019 (https://iris.who.int/handle/10665/336323).

See for further information: https://www.who.int/teams/health-care-readiness/clinical-management-of-monkeypox

World Health Organization

Appendix 8: Mpox lesions differential diagnosis

Mpox lesions differential diagnosis



Primary syphilis lesion
Credit: CDC/Dr NJ Fiumara



Secondary syphilis rash
Credit: WHO Photo library

The following diseases have similar lesions to mpox.

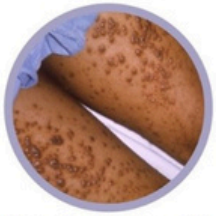
Syphilis

Primary: non painful solitary lesion in genitals.

Secondary: non painful generalized skin and mucocutaneous lesions.



Varicella (chicken pox)
Credit: CDC/Dr John Noble, Jr.



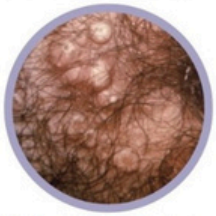
Varicella (chicken pox)
Credit: CDC/Dr John Noble, Jr.

Varicella

The lesions go through several stages, turning into fluid-filled blisters before forming a scab and falling off. They will appear quickly and at different stages and different times.



Molluscum contagiosum
Credit: CDC/Jim Pledger



Molluscum contagiosum
Credit: CDC

Molluscum contagiosum

No prodromal symptoms and takes on a more chronic time course, with most infections self-resolving in 6 to 12 months.



Herpes simplex
Credit: CDC/ Dr Thomas F Sellers, Emory University



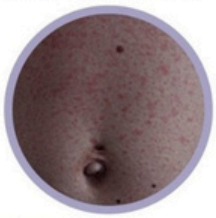
Herpes simplex
Credit: Kieron Leslie, University of California San Francisco, USA

Herpes simplex

There are normally multiple previous oral or genital herpes attacks. They progress from vesicles to erosions and ulcerations, while mpox lesions progress to firm pseudopustules.



Measles
Credit: CDC/Betty G Partin



Rash in measles
Credit: WHO library

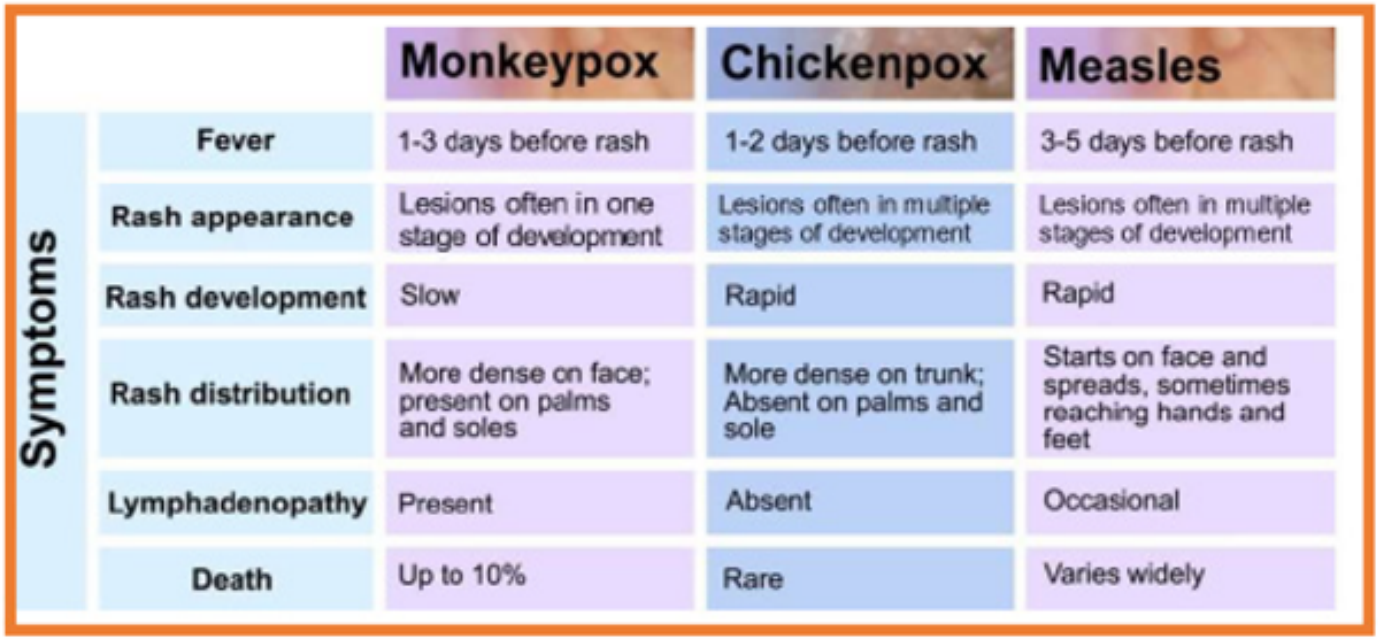
Measles

- Koplik's lesions in mouth.
- Red eyes.
- Start on forehead with red blotchy rash.

World Health Organization

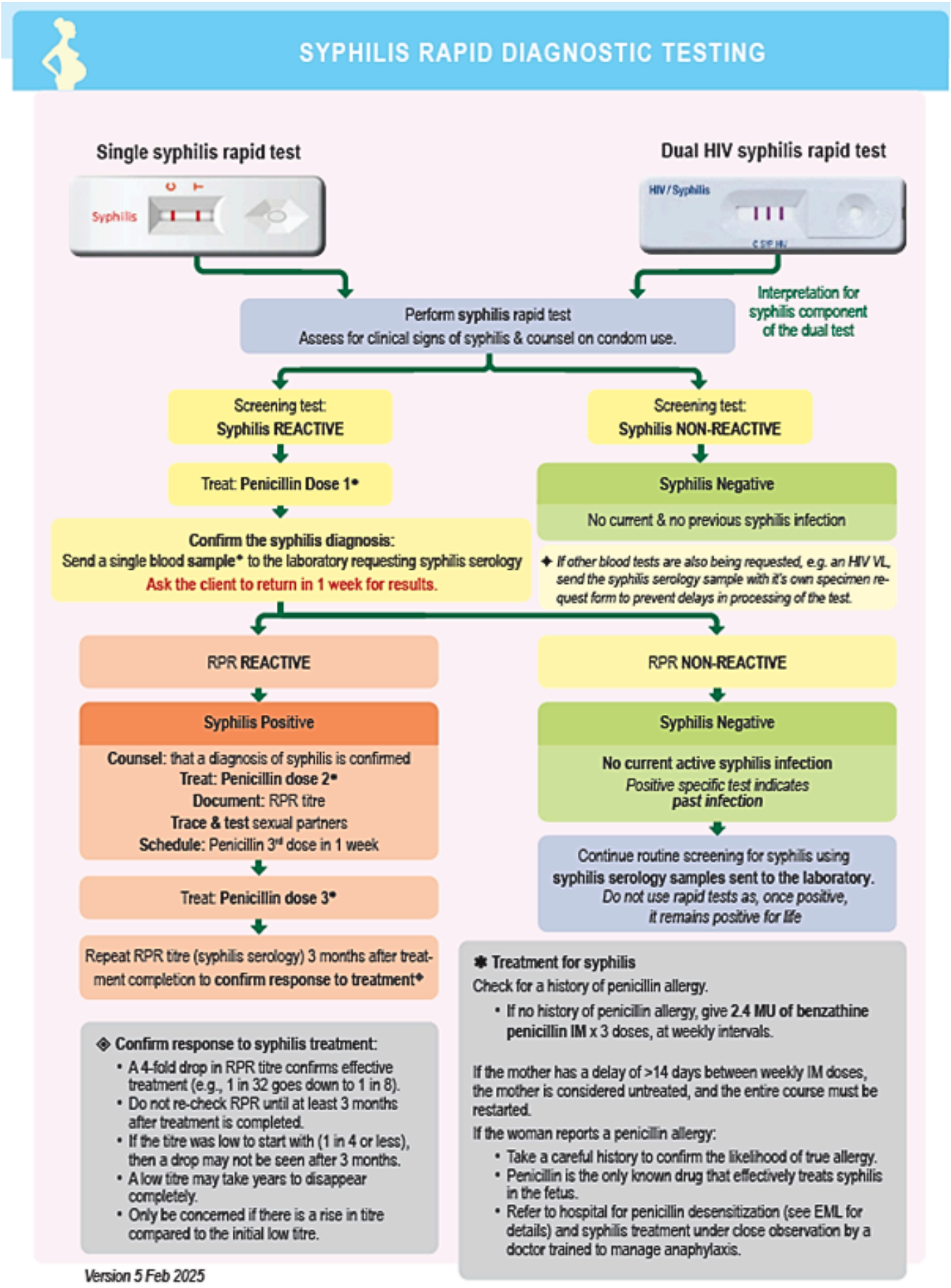
Comparison between Mpox, Chickenpox and Measles

Figure 4: Comparing Mpox and other Vesicular Skin Lesions

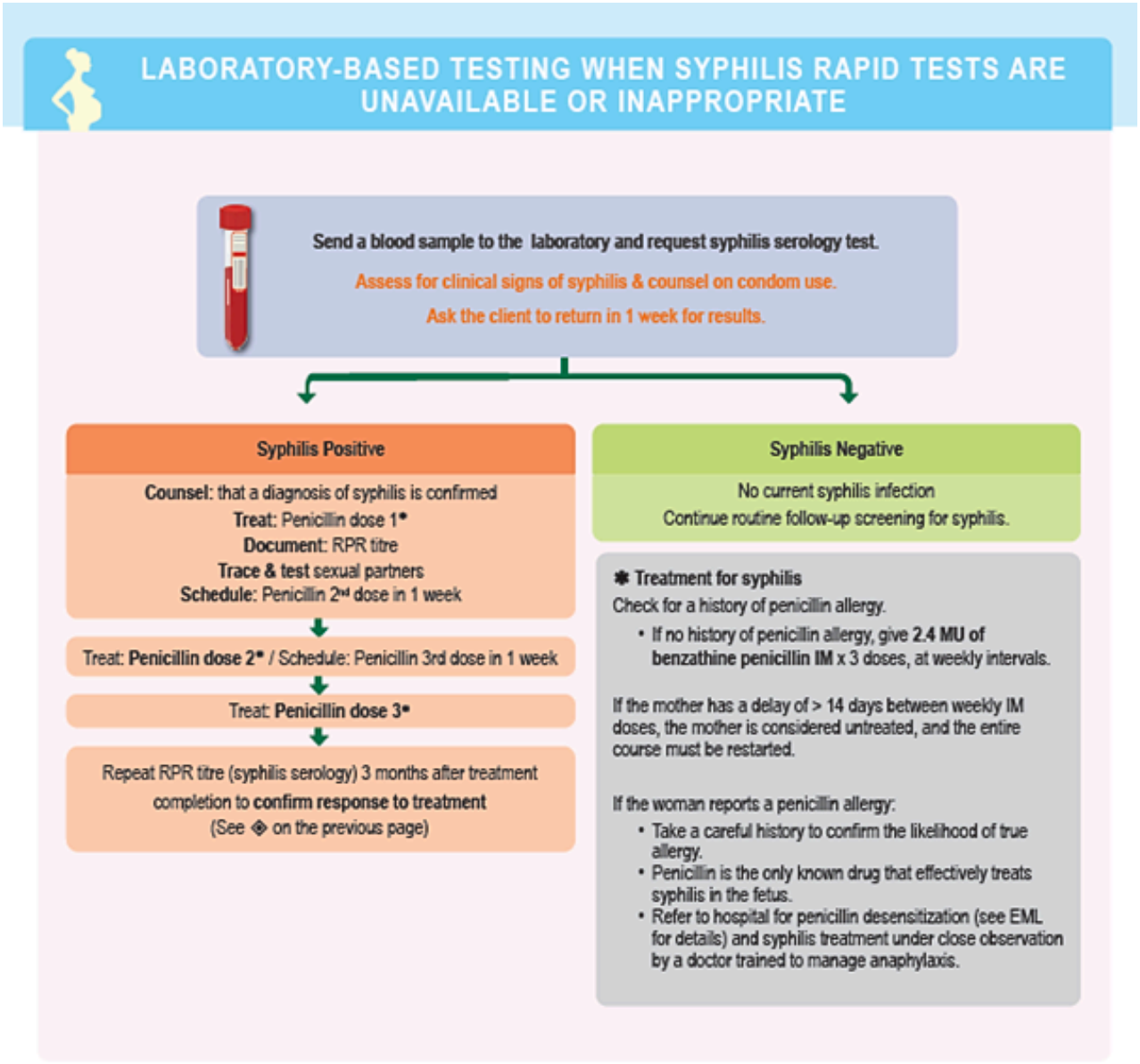


		Monkeypox	Chickenpox	Measles
Symptoms	Fever	1-3 days before rash	1-2 days before rash	3-5 days before rash
	Rash appearance	Lesions often in one stage of development	Lesions often in multiple stages of development	Lesions often in multiple stages of development
	Rash development	Slow	Rapid	Rapid
	Rash distribution	More dense on face; present on palms and soles	More dense on trunk; Absent on palms and sole	Starts on face and spreads, sometimes reaching hands and feet
	Lymphadenopathy	Present	Absent	Occasional
	Death	Up to 10%	Rare	Varies widely

Appendix 9: Syphilis & HIV Testing and Management during Pregnancy



Appendix 10: Syphilis Laboratory-Based Testing during Pregnancy



TREATING PARTNERS

- Trace and test partners of women with confirmed syphilis
- Test the partner using a rapid syphilis test if available and assess for symptoms and signs of a genital ulcer or secondary syphilis.
- If the rapid test is positive, and symptoms or signs of syphilis are present, treat the partner for early syphilis using one of the following options:
  - A single immediate dose of benzathine penicillin 2.4 MU IM, if stock levels are sufficient
  - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 14 days
- If the rapid test is positive and there are NO symptoms or signs of syphilis, send a confirmatory blood sample to the laboratory for a syphilis serology test. Do not wait for the results before treating the partner, but be sure to check the results 1 week later. If the confirmatory test is positive, treat the partner for latent syphilis using one of the following options:
  - Benzathine penicillin 2.4 MU IM, once weekly for 3 weeks, if stock levels are sufficient
  - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 30 days

Source: Guideline for vertical transmission prevention of communicable infections (2023).

Appendix 11: Care of skin lesions in mpox infection

Care of skin lesions in mpox infection

1 Assessment



Conduct a full body skin examination, including mucosas (conjuntiva, oral, rectal and genital regions)

2 General treatment principles

A



Hand hygiene with soap and water or sanitizer, especially before and after touching lesions or contaminated surfaces (see hand hygiene: Why, How and When?)

B



As a patient with mpox: avoid touching lesions where possible to reduce autoinoculation

C



As a health worker: use personal protective equipment (PPE) to be in close contact (e.g. cleaning and dressing) with the lesions of a patient with mpox: gloves, gown, medical mask and eye protection.

3 Non complicated lesions

A



If lesions are macules, pustules, vesicles: clean the area with water and soap and dry the skin with a clean towel to keep them clean and dry

B



Cover the lesions with clean dry bandages to reduce the transmission if in close proximity with other people.

C



If lesions are crusted: use gauze impregnated with petroleum jelly over the lesions

D



If lesions are itchy: use emolients or lotions made of calamine mineral over the lesions

4 Complicated lesions

A



If Oral mucosal lesions: use alcohol-free mouthwash or saline solution to clean the mouth

B



If mucosal painful lesions: apply topical anaesthetic gel to affected area(s) as needed.

C



If Eroded/macerated lesions: soak lesions for 20 minutes in a solution of dilute potassium permanganate and clean water to a concentration of 1 in 10,000 or iodine to clean, disinfect and prevent superinfection.

D



For superinfection of skin lesions: extreme redness, tenderness, pus or extensive disseminated mpox lesions, consult with clinician or Infectious diseases specialist to initiate treatment with antibiotics.

5 Follow up



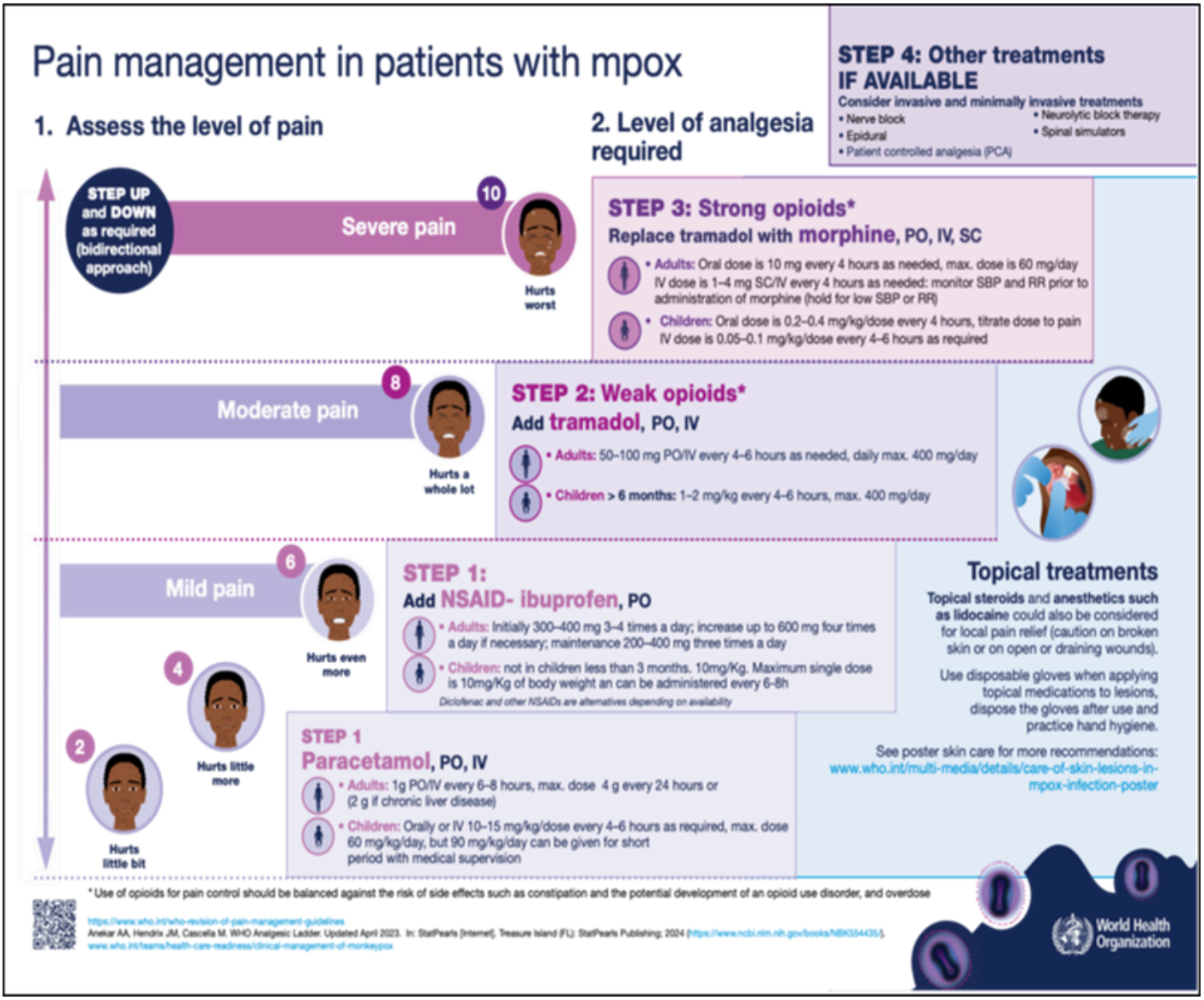
After healing, there may be some dyspigmentation in affected areas this may resolve in 6-18 months. Sunscreen may prevent further dyspigmentation.

See for further information: www.who.int/teams/health-care-readiness/clinical-management-of-monkeypox

Infection prevention and control and water, sanitation and hygiene measures for home care and isolation for mpox in resource-limited settings: interim operational guide. Geneva: World Health Organization; 2024 (https://iris.who.int/handle/10665/379477).

World Health Organization

Appendix 12: Pain management in patients with mpox



REFERENCES

Dalton AF, Diallo AO, Chard AN, et al. (2023). Estimated Effectiveness of JYNNEOS Vaccine in Preventing Mpox: A Multijurisdictional Case-Control Study — United States, August 19, 2022–March 31, 2023. MMWR Morb Mortal Wkly Rep 72:553–558. DOI: 10.15585/mmwr.mm7220a3.

IPC Standard Operating Procedure for Healthcare Management of Mpox Patients. National Department of Health, South Africa Access https://www.nicd.ac.za/wp-content/uploads/2023/03/IPC-SOP-For-mpox-management.pdf (As on 13 June 2024).

Liverpool University Hospital. Tecovirimat as treatment for patients hospitalized due to monkeypox virus infection-Standard Operating Procedure (SOP), shared via email

Mental Health Act (Act 17 of 2002) of South Africa. Access at: https://www.gov.za/sites/default/files/gcis_document/201409/a17-02.pdf (As on 13 June 2024).

Savoy et al. 2020, Sexual health history: techniques and tips. Am Fam Physician. 2020;101(5):286-293

South African Adult Hospital Level and Paediatric Hospital level Essential Medicines List: Access at: https://www.health.gov.za/nhi-edp-stgs-eml/

South African Tertiary Level Essential Medicines List: Access at: https://www.health.gov.za/nhi-edp-stgs-eml/

WHO, Clinical management and infection prevention and control of monkeypox, Interim rapid response guidance 10 June 2022. Access at: https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1. (As on 20 June 2024).

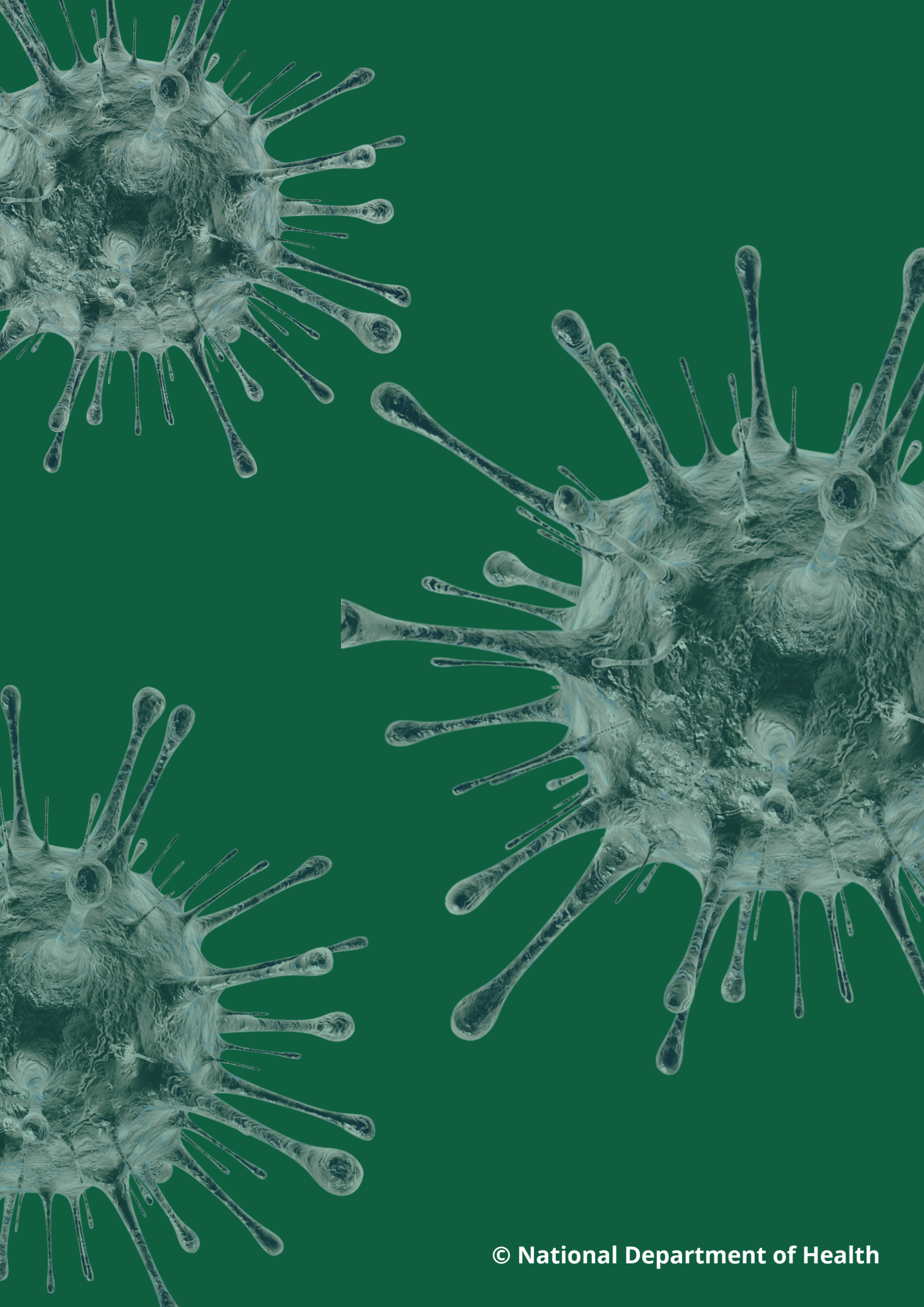
WHO mpox outbreak toolbox. Access at: https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/mpox-outbreak-toolbox (As on 13 June 2024)

WHO, Diagnostics testing for monkeypox virus, interim guidance, May 2024. Access at: https://iris.who.int/bitstream/handle/10665/376952/WHO-MPX-Laboratory-2024.1-eng.pdf?sequence=1 (As on 5 July 2024)

Yinka-Ogunleye A, Aruna O, et al. 2019. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Lancet Infect Dis. 19(8):872-879. DOI: 10.1016/S1473-3099(19)30294-4.

The PALM007 Writing Group. Tecovirimat for clade 1 MPXV Infection in the Democratic Republic of Congo. New England Journal of Medicine 2025; 393:1484-1496.

NIAID Blog. The STOMP Trial Evaluates an Antiviral for mpox: https://www.niaid.nih.gov/news-events/stomp-trial-evaluates-antiviral-mpox



© National Department of Health