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Chapter 6 – MPOX Clinical Management of Cases (Therapeutic Options)

Please note that this document should be used in tandem with other **MPOX Algorithms and Guidance documents.**

Readers should not rely solely on the information contained with these guidance outputs. Guidance information is not intended to be a substitute for advice from other relevant sources including and not limited to, the advice from a health professional. Clinical judgement and discretion will be required in the interpretation and application of this guidance document. This guidance document is under constant review based upon emerging evidence at national and international levels and national policy decisions.

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1.0	23/07/2025	*De novo* guideline development due to the emergence of the new monkeypox virus clade Ib and a resurgence of cases in the African region, a World Health Organization (WHO) Public Health Emergency of International Concern (PHEIC) was once again declared on 14 August 2024.
1.1	06/05/2026	Update to disclaimer re: EMA 2026 review on tecovirimat

DISCLAIMER

These guidelines outline Ireland's national human mpox treatment guidelines. The intention of these guidelines is to reflect the current available evidence base. Readers should not rely solely on the information contained within these guidelines. Guideline information is not intended to be a substitute for advice from other relevant sources, including, but not limited to, advice from Consultants in Infectious Diseases (Adult or Paediatric), Clinical Microbiology or other medical specialities providing direct patient care. Clinical judgment and discretion may be required in the interpretation and application of these guidelines.

Important Notice (Interim Position Pending Full Guideline Review)
Following recent review (March 2026) by the European Medicines Agency (EMA), tecovirimat is no longer recommended for the routine treatment of mpox, based on current clinical trial evidence demonstrating no significant benefit in time to lesion resolution, symptom control, or virological outcomes in patients with established disease.

However, it is acknowledged that:

- Current evidence is primarily derived from studies **in immunocompetent adult populations with generally mild-to-moderate disease**,
- **Immunocompromised individuals and patients with severe disease are under-represented**, and
- Treatment in clinical trials was typically initiated l**ater in the disease course**, which may limit observed efficacy.

In this context, and pending further national review, **off-label tecovirimat may be considered on a case-by-case basis**, where:

- The patient has severe mpox, or is at high risk of severe disease (e.g. significant immunosuppression), and
- There is multidisciplinary discussion, including Infectious Diseases (Adult or Paediatric), Genitourinary Medicine specialists, or Maternal-Fetal Medicine specialists.

Use in such circumstances should be:

- Undertaken within a **clearly documented clinical governance framework**,
- Based on an **individualised risk–benefit assessment**, and
- Recognised as occurring in a setting of **uncertain clinical efficacy**.

This interim position aims to support **prudent clinical decision-making** while ensuring alignment with evolving international evidence and regulatory guidance.

TABLE OF CONTENTS

1 INTRODUCTION 5

1.1 PURPOSE 5
1.2 SCOPE 5
1.3 TARGET 5
1.4 BACKGROUND INFORMATION 5
1.4.1 Epidemiology 6
1.4.2 Information of cell cycle and pathogenesis as related to therapeutics 7
1.5 THERAPEUTIC OPTIONS 7
1.5.1 Skin Lesion Care and Infection Prevention 7
1.5.2 Counselling of Patients 7
1.5.3 Infection Prevention and Control (IPC) Measures 8
1.5.3.1 Standard Considerations: 8
1.5.3.2 Additional Information 8
1.5.4 Antiviral & Other Therapy Options 9
1.5.4.1 Antiviral therapeutics 9
1.5.4.2 Alternative therapeutics 16
1.5.5 Vaccination 22
1.5.6 Public Health Management 22
1.5.6.1 Contact Tracing 22
1.5.6.2 Reporting Requirements 22

2 REFERENCES 23

3 ADDITIONAL RESOURCES 26

4 APPENDIX A 27

4.1 CONTACT DETAILS FOR RELEVANT HEALTH SERVICES AND LABORATORIES 27

5 APPENDIX B 28

5.1 ADDITIONAL RESOURCES FOR HEALTHCARE PROVIDERS AND PATIENTS 28

6 APPENDIX C 29

6.1 SUMMARY OF THERAPEUTIC OPTIONS 29

1 INTRODUCTION

1.1 Purpose

The purpose of these guidelines is to outline the current therapeutic options for the prevention and management of human mpox virus (MPXV) infection. These guidelines will be reviewed as the mpox situation evolves and as therapeutic options change.

1.2 Scope

- This guidance focuses on the treatment options for patients with confirmed mpox.
- This guidance further provides pharmacological options for post-exposure prophylaxis (PEP) in those at risk of severe complications following mpox exposure (e.g., severely immunocompromised).
- This guidance does not elaborate on the diagnostic work-up and clinical management of patients prior to the confirmation of mpox or vaccine-related complication.
- For further information on diagnostic workflow see **here**.
- For further information on vaccination see **here** (mpox chapter).
- For further information on public health response guidance see **here**.

1.3 Target

This guidance document is intended for healthcare professionals, including physicians, nurses, and pharmacists, involved in the treatment, and management of mpox. It is also relevant for public health officials, laboratory personnel, and policymakers responsible for developing and implementing mpox-related health strategies. The document aims to provide therapeutic options to ensure effective and safe management of mpox cases across diverse healthcare settings.

1.4 Background Information

Mpox is a **viral zoonotic disease** that is caused by the MPXV virus. There are 2 distinct clades of MPXV, clade I and clade II. Mpox was previously classified as a high consequence infectious disease (HCID)[1]. In January 2023, the HCID Clinical Advisory Group (CAG) advised that clade II mpox no longer met the criteria for an HCID. In May 2025, the HCID CAG recommended that clade I mpox should no longer be classified as an HCID. This guidance therefore covers the contacts of all cases of mpox, irrespective of clade, and replaces the clade specific contact tracing guidance previously published.

An mpox case is defined as a case that meets the confirmed or highly probable **case definition** [1].

[1] **HCID:** High consequence infectious disease (HCID is defined as: an acute infectious disease; typically having a high case-fatality rate; not always having effective prophylaxis or treatment; often difficult to recognise and detect rapidly; able to spread in the community and within healthcare settings; and requiring an enhanced, individual, population, and system response to ensure it is managed effectively, efficiently and safely.

Health professionals undertaking the risk assessment should take into account the extent of lesions at the time of exposure, as the risk of transmission will be higher if there are widespread uncovered lesions on uncovered areas (for example, hands or face) compared with, for example, a small number of localised genital lesions or if the case was displaying respiratory symptoms at the time of contact, compared to an asymptomatic or pre-symptomatic individual. Contact(s) who are within twenty-one days of exposure to confirmed case of mpox should be advised by the healthcare professional/s to inform any healthcare facility of this exposure when they present for medical assessment/treatment.

1.4.1 Epidemiology

The first human case was recorded in 1970 in the Democratic Republic of the Congo (DRC). Since then the infection has been reported in a number of African countries and, more recently, has spread to multiple countries around the world. This includes cases in Ireland.

There are 2 major types of MPXV. These are called clades and are known as clade I and clade II. Clade I was previously known as Central African or Congo basin clade, after the places it was originally found. Clade II was previously known as West African clade.

Sub-types of each clade have been identified. Clade I is split into clade Ia and clade Ib. Clade II is split into clade IIa and clade IIb. These can be broken down further into groupings called lineages. This is important as we can track different outbreaks of mpox around the world by looking at the exact type of the mpox viruses involved.

Historically, mpox was known to have been occasionally passed on from infected animals to humans, with humans sometimes passing it on to other people that they had close contact with. Since May 2022 however, cases of human mpox have been reported in multiple countries that have not previously had MPXV in animal or human populations. This has included cases in the UK. This ongoing outbreak is mostly caused by clade IIb, lineage B.1 MPXV, and is spread mostly by sexual contact.

Since August 2024, clade I MPXV has also been reported from multiple countries outside of the African region that had not previously reported it, including cases in Europe. This is mostly caused by clade Ib MPXV, and is spread mostly through close physical contact (including both sexual and non-sexual contact).

Information of Irish epidemiology is available **here** [2].

Information regarding the global distribution of reported mpox clades and a list of “at risk” countries is available **here** [3].

1.4.2 Information of cell cycle and pathogenesis as related to therapeutics

Mpox virus (MPXV) is an orthopox virus in the same family as smallpox(variola) and vaccinia. It is a DNA virus which enters the human cell by fusion or endocytosis after binding on to surface glycosaminoglycans. Replication occurs entirely in the host cell cytoplasm. Large genomes code for the many enzymes required for replication independent of the host nucleus, with virions also carrying ready formed protein. As a result, viral assembly is complex and is therefore an attractive anti-viral target. Orthopox virus genomes contain large regions dedicated to modulation of the host immune system including inhibition of pro-inflammatory cytokines. [4]

1.5 Therapeutic Options

1.5.1 Skin Lesion Care and Infection Prevention

For comprehensive guidance on managing skin lesions, preventing secondary infections, and addressing complications, refer to the World Health Organization (WHO) **here**. [5] Key recommendations include:

- **General Care:** Keep lesions clean, dry, and exposed to air. Clean gently with sterile water or antiseptic.
- **Infection Prevention:** Avoid scratching. Monitor for signs of bacterial infection. Antibiotics are only recommended if secondary infection is confirmed— For current prescribing guidance, clinicians should refer to **antibioticprescribing.ie**, the national resource for antimicrobial prescribing in community settings in Ireland or local hospital antimicrobial prescribing resources for acute hospital settings.
- **Managing Complications:** For issues like exfoliation or abscesses, maintain hygiene and consult healthcare professionals for appropriate interventions, including incision and drainage when necessary.

1.5.2 Counselling of Patients

Patients should be provided with clear, accessible information to support self-care, reduce anxiety, and prevent complications. Key counselling points include:

- **Skin Lesion Care**: Advise patients to keep lesions clean and dry, avoid scratching, and monitor for signs of secondary infection.
- **When to Seek Help**: Educate patients on symptoms that warrant medical review, such as increasing pain, pus, or fever.
- **Infection Prevention**: Reinforce hand hygiene and safe disposal of dressings or materials that come into contact with lesions.
- **Mental Health and Stigma**: Acknowledge the potential psychological impact of mpox and signpost to support services if needed.
- **Access to Reliable Information [6]** Refer patients to trusted resources such as the **HPSC mpox information page**.

1.5.3 Infection Prevention and Control (IPC) Measures

1.5.3.1 Standard Considerations:

- For detailed infection prevention and control measures, refer to the guidance document: ***Infection Prevention and Control Precautions for Healthcare Workers in the Management of Suspected or Confirmed Mpox (Clade I and Clade II)*** - found **here**.

1.5.3.2 Additional Information

- Ensure that for all clinical interactions with MPXV cases (i.e. confirmed and probable) that personal protective equipment (PPE) is used in line with **National Irish IPC guidance**. [7]

1.5.4 Antiviral & Other Therapy Options

1.5.4.1 Antiviral therapeutics

There is no medication that is effective in curing mpox disease, however anti-viral strategies are under investigation for safety and efficacy in preventing morbidity and mortality. Most people will fully recover with supportive care, but patients who are severely immunocompromised or have certain skin disorders are at particular risk of severe disease. Although randomised controlled trials are lacking for these patient groups, anti-viral strategies are recommended on a risk benefit basis.

TECOVIRIMAT PRESCRIBING GUIDANCE (Please refer to Summary of Product Characteristics (SPC) of Tecoviramat for full prescribing information)	
Drug Name	Tecovirimat SIGA
Mechanism of action	Tecovirimat inhibits the activity of the orthopoxvirus VP37 protein, which is encoded by a highly conserved gene in all members of the orthopoxvirus genus. Tecovirimat blocks the interaction of VP37 with cellular Rab9 GTPase and TIP47, which prevents the formation of egress competent enveloped virions necessary for cell-to-cell and long-range dissemination of virus.
Background	Prior to the 2022 clade IIb outbreak, efficacy of tecovirimat had only been studied in rabbits and non-human primates. These studies demonstrated that tecovirimat prevented death in 80 to 100% of animals when administered up to and including 5 days post Mpox infection [8]. This survival rate reduced to 50% when treatment was initiated 6 days after infection. Phase 2 studies of tecovirimat in healthy human volunteers demonstrated safety. One randomized controlled trial of 107 healthy volunteers showed the most common side effects to be nausea and headache [9]. In another phase 2 trial of 30 volunteers, side effects were only experienced at the highest dose tested and included GI upset, dry mouth and headache [10]. Although one human study with 40 patients recorded two instances of neutropaenia, these were not thought to be drug related [11]. The largest trial up until then to assess safety in humans recruited 449 healthy volunteers and assigned 361 to tecovirimat at a dose of 600mg twice daily for 14 days. 1.1% experienced at least a grade 3 side effect, with headache being the most common symptom [12]. Pharmaceutical data highlights two drug interactions namely a risk of hypoglycaemia when tecovirimat is co-administered with repaglinide and a decrease in midazolam effectiveness [13]. Since the 2022 global outbreak, two major randomised controlled trials have been conducted. Broadly, they confirmed that tecovirimat has a favourable safety profile, but they did not demonstrate efficacy for reduction of mortality or decrease in duration of symptoms.

	The NIH funded STOMP trial (Study of Tecovirimat for Human Mpox Virus) compared a placebo control to a blinded tecovirimat arm in people experiencing recent onset Mpox with a low risk of severe disease (https://clinicaltrials.gov/study/NCT05534984). It recruited patients across the US, South America, Japan and Thailand with confirmed MPXV clade 2 infection. Tecovirimat did not reduce symptom duration or have an effect on pain. [14] The PALM007 trial (https://clinicaltrials.gov/study/NCT05559099) was jointly funded by the National Institute of Allergy and Infectious Diseases and the Institut National de la Recherche Biomedicale and studied tecovirimat versus placebo intervention arms. [15] They enrolled 597 participants with confirmed clade 1 mpox in the DRC. Tecovirimat was well tolerated but did not show efficacy towards reduction in mortality or speed of lesion resolution. The study's 1.7% overall mortality rate was lower than the 3.6% reported in the general population locally, and suggests that high quality supportive care is a key management approach. An evaluation of data reported to CDC as part of their expanded access program included 7100 patients treated with tecovirimat. It showed good tolerability, but noted that immunosuppressed patients experienced more side effects. The most common indications for tecovirimat use were anogenital lesions (84%) and pain (53%). Most began treatment within one week of symptoms and recovered after a standard 14-day course. They reported 223 serious adverse effects and 40 deaths. [16] The potential for resistance to tecovirimat is a notable concern, with drug selected mutations in VP37 already being reported in immunosuppressed individuals. Viruses harbouring VP37:N267del, for example, were shown to correspond to an 85-to-230-fold decrease in susceptibility compared to wild type. Resistance has been demonstrated longitudinally in immunosuppressed patients on tecovirimat, and transmission of tecovirimat resistant virus has also been documented. However, it is estimated that individuals with a tecovirimat resistant virus represent less than 1% of the total number of patients who have received tecovirimat in the US. Further research is needed to examine efficacy in specific patient sub-groups, timing of intervention in relation to symptom onset, and severity of clinical disease.
Clinical prioritisation	Tecovirimat should only be initiated following discussion with an ID or GUM consultant in a tertiary centre accustomed to managing these patients.

Tecovirimat should be considered in patients who have evidence of severe disease or are at risk of severe disease .

Severe disease:

1. Haemorrhagic disease, confluent lesions, encephalitis, pneumonitis;
2. Eye Disease;
3. Numerous Lesions (> 100);
4. Severe local disease; and
5. Other conditions requiring hospitalisation excluding admission for isolation purposes only.

Persons at risk of severe disease:

1. Immunocompromised **
2. Paediatric especially < 12 years;
3. Pregnancy/Breast Feeding; and
4. Atopic Dermatitis or other skin disease.

Where supply is limited tecovirimat should be used according to priority group order.

PRIORITY	DETAILS
HIGH	• Life threatening disease (encephalitis, pneumonitis); • Eye disease; and • Numerous lesions (>100) in immune compromised or children.
MEDIUM	• Numerous lesions (>100) in all other patients; and • Severe local disease in immunocompromised or < 12 years old.
LOW	• Severe local disease general population.

**Immunocompromising conditions e.g. HIV/AIDS (detectable VL and/or CD4 < 200), Leukaemia, Lymphoma, Generalised malignancy, solid organ transplantation, recent chemotherapy/immunotherapy/high dose steroids, Haematopoietic stem cell transplant recipient, autoimmune disease with immunodeficiency as clinical component.

Fertility, Pregnancy & Lactation considerations

Fertility

- The effects of tecovirimat on fertility in humans have not been studied.

Paediatric considerations	**Pregnancy** • Pregnant women may be more vulnerable to the adverse effects of mpox and liable to more severe symptoms as well as risks to the fetus, including miscarriage, fetal death and preterm birth. • Pregnant women are a risk group that should be considered for Tecovirimat following a risk benefit discussion. • There are no adequate studies conducted on pregnant women. No embryofetal developmental toxicity was observed in animal studies during the period of organogenesis. • There are limited human data available for tecovirimat, and pregnancy outcome data from animals following tecovirimat exposure is more reassuring. Therefore, tecovirimat may be preferred for use by pregnant women with mpox. [16] • The decision to treat should involve Maternal-Fetal medicine consultation. • Pregnant women with severe mpox infection (and, given expected severity, this includes suspected clade I cases) or complex obstetric conditions should be admitted to hospital - this is a tertiary hospital or designated centre (e.g. Mater/ CUMH). **Lactation [18]** • It is unknown whether tecovirimat/metabolites are excreted in human milk. • Available toxicological/safety data in animals have shown excretion of tecovirimat in milk. • A risk to the newborns/infants cannot be excluded. • Breast-feeding should be discontinued during treatment with tecovirimat. • Data from previous outbreaks suggest that the risk of severe disease with mpox infection is increased in children, particularly in the first year of life. • All children with mpox infection should be discussed with the Paediatric Infectious Disease service in Children's Health Ireland. • Tecovirimat is authorised for use in children weighing over 13kg with dosing listed below. • Dosing has not yet been established for children under 13kg however given the high risk nature of this group, and ongoing research into this area, options should be discussed with the Paediatric Infectious Diseases service in Children's Health Ireland (CHI).
Formulation	**Tecovirimat SIGA 200 mg hard capsules.** • Each hard capsule contains tecovirimat monohydrate equivalent to 200 mg tecovirimat. • Contains lactose

Route of administration

- In time, intravenous formulation may become available in Ireland and guidance will be updated at that time.

Oral use only.

Tecovirimat treatment should be initiated as soon as possible after diagnosis.

Dose and duration of therapy

For adults and children of at least 13 kg, the recommended doses are described in Table below.

BODY WEIGHT	DOSAGE	NUMBER OF CAPSULES
13 kg to less than 25 kg	• 200mg every 12 hours for 14 days	• One Tecovirimat 200 mg capsule
25 kg to less than 40 kg	• 400mg every 12 hours for 14 days	• Two Tecovirimat 200 mg capsules
40 kg to less than 120 kg	• 600 mg every 12 hours for 14 days	• Three Tecovirimat 200 mg capsules
120 kg and above	• 600mg every 8 hours for 14 days	• Three Tecovirimat 200 mg capsules

Re-dosing in case of vomiting

- If vomiting occurs within 30 minutes of taking tecovirimat hard capsules, another dose may be administered immediately.
- If vomiting occurs more than 30 minutes after taking tecovirimat hard capsules, no additional dose should be given and dosing should resume as usual after 12 hours.

Elderly

No dose adjustment required.

Renal impairment

No dose adjustment required, but caution in patients with severe renal impairment.

Hepatic impairment

No dose adjustment required, but caution in patients with severe hepatic impairment.

Method of administration	**Paediatric population** Tecovirimat should not be administered to children of less than 13 kg body weight as no dosing recommendations have been established. As above all cases of paediatric mpox, including children under 13 kg, should be discussed with CHI Oral use. Tecovirimat hard capsules should be taken within 30 minutes after a meal of moderate or high fat (~ 600 calories and ~ 25 grams of fat). **For patients who cannot swallow:** • Tecovirimat hard capsules, the capsules may be opened and the contents may be mixed with approximately 30 mL of liquid (e.g. milk) or soft food (e.g. yogurt) and swallowed within 30 minutes of completing a meal of moderate or high fat.
Drug-drug interactions	**Effect of other medicinal products on Tecovirimat** • Tecovirimat is a substrate of UGT1A1, 1A3 and 1A4. Co-administration of tecovirimat with strong inhibitors or inducers of these UGTs is not expected to have a clinically important effect on tecovirimat exposures. **Effect of Tecovirimat on other medicinal products** • Tecovirimat and its M4 metabolite are inducers of cytochrome P450 (CYP)3A and CYP2B6. Co-administration with tecovirimat may lead to reduced plasma exposures of sensitive substrates of CYP3A4 or CYP2B6, potentially leading to reduced effects. Monitoring is advised during co-administration of tecovirimat with CYP3A4 and CYP2B6 substrates that have narrow therapeutic windows. • Tecovirimat is a weak inhibitor of CYP2C8 and CYP2C19. Co-administration with tecovirimat may lead to increased plasma exposures of sensitive substrates of CYP2C8 or CYP2C19, potentially leading to increased adverse effects. Monitoring is advised during co-administration of tecovirimat with CYP2C8 and CYP2C19 substrates that have narrow therapeutic windows. **Refer to drug interaction resources on how to minimise these drug interactions.**
Adverse effects	Common symptoms include: • Dizziness; • Headache (12.3%) • Abdominal pain (upper);

	• Abdominal discomfort; • Diarrhoea; • Nausea (4.5%); and • Vomiting.

1.5.4.2 Alternative therapeutics

Alternative therapeutic approaches have been reported in the literature and are based on in vitro data. They have not been tested with randomised controlled trials in human populations. They should only be used under the guidance of an expert infectious diseases specialist, or ideally under a research framework. They are reserved for cases where there are concerns regarding severity of disease, severity of immune compromise, or resistance to tecovirimat. Their side effect profile is much poorer than that of tecovirimat.

VACCINIA IMMUNE GLOBULIN INTRAVENOUS (VIGIV) PRESCRIBING GUIDANCE **(Please refer Centers for Disease Control and Prevention (CDC) Expanded Access Protocol of VIGIV for full prescribing information)** ***Vaccinia Immune Globulin (VIG) is not routinely stocked and access in Ireland would likely need to be coordinated through national public health authorities, potentially in collaboration with international partners such as the CDC or WHO. This may require early exploration and planning to ensure availability in the event of clinical need.***	
Drug Name	Vaccinia Immune Globulin Intravenous (VIGIV, CNJ-016) [19]
Mechanism of action	There are published VIGIV clinical use data for vaccinia-related infections. The existence of shared serologic cross-reactivity between the OPXVs, and the ability of neutralizing antibodies to one OPXV to partially neutralize the infectivity of other members of the genus OPXV, speculates potential clinical benefit by the use of VIGIV for viral neutralization in instances where active replication of an OPXV other than variola and vaccinia is occurring. [19]
Background	Orthopoxviruses (OPXVs) in the Poxviridae family comprise the following species which can infect humans: variola virus, vaccinia virus (the virus in smallpox vaccine ACAM2000 and smallpox/mpox vaccine JYNNEOS), monkeypox virus (MPXV), cowpox virus, Akhmeta virus, and Borealpox virus (formerly known as Alaskapox virus). Variola virus causes smallpox in humans exclusively while the other viruses cause zoonotic infections that can also be transmitted person-to-person. Infections by OPXVs, such as mpox (formerly known as monkeypox) may be localised to the skin or disseminated along the mucosal surface or the respiratory tract. Infected persons may present with serious illnesses including, but not limited to encephalitis, severe inflammatory response syndrome, respiratory failure, painful lymphadenopathy of head or neck with/without associated dysphagia or compromised airway, extensive dermal disruption during rash phase, and other septic syndromes. After the World Health Organization announced global eradication of smallpox in 1979, the routine use of vaccinia virus smallpox vaccine was nearly eliminated; certain U.S. military personnel and persons at risk for occupational

	exposure to OPXV are recommended to receive smallpox and/or mpox vaccine per the **Advisory Committee on Immunization Practices** (ACIP) recommendations. [20] There are two vaccines approved by the Food and Drug Administration (FDA) for OPXV infections: ACAM2000 (replication-competent, live vaccinia vaccine approved for smallpox for adults and children) and JYNNEOS (replication-deficient, Modified Vaccinia Ankara-Bavarian Nordic [MVA-BN] approved for smallpox and mpox in adults 18 years and older). ACAM2000, given it is a replication-competent live vaccinia virus vaccine, carries a risk for serious adverse events (e.g., progressive vaccinia and eczema vaccinatum), for which treatment with vaccinia immune globulin intravenous (VIGIV) and antivirals may be used. Virulent OPXVs including variola virus and MPXV pose a public health concern given the potential for rapid transmission especially among unvaccinated populations. Currently, there are no available treatments for mpox approved by FDA. However, antivirals and other medical countermeasures (MCMs) developed by the U.S. government for smallpox preparedness may be beneficial against mpox. The stockpiled MCMs available as treatment options for mpox in the Strategic National Stockpile (SNS) include intravenous (IV) and oral (PO) tecovirimat (TPOXX), and VIGIV. Despite the paucity of information on VIGIV efficacy against mpox, the presumed potential clinical benefit is that the antibodies against vaccinia virus present in VIGIV might provide passive immunity against mpox based on serologic cross-reactivity between OPXVs. [21] Comparison of mpox virus genome sequences in the 2022 outbreak to those of vaccinia virus suggests that vaccinia virus-based vaccines induced immunogenicity which was highly cross-reactive against mpox virus. [22] Use of VIGIV as treatment of OPXV infections, especially in severe manifestations of mpox observed in immunocompromised patients during the 2022 mpox outbreak, may be clinically necessary. VIGIV should only be initiated following discussion with an ID or GUM consultant in a tertiary centre accustomed to managing these patients.
Clinical indications	**Mpox treatment should be considered for use in patients who have clinical manifestations of:** • Severe disease (e.g., haemorrhagic disease, large number of lesions, necrotic lesions, severe lymphadenopathy, involvement of multiple organ systems and associated comorbidities, other conditions requiring hospitalisation) ; and

Pregnancy & Lactation considerations	• Involvement of anatomic areas which might result in serious sequelae that include scarring or strictures; anorectal lesions interfering with bowel movements; and severe infections, especially those that require surgical intervention such as debridement. Treatment should also be considered for use in patients who are at high risk for severe disease: • Persons with severe immunocompromise 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 haematopoietic stem cell transplant < 24 months post-transplant or ≥ 24 months but with graft-versus-host disease or disease relapse, or having autoimmune diseases with immunodeficiency as a clinical component • Children, particularly younger than 8 years of age; • Pregnant or breastfeeding women; and • Persons with a condition affecting skin integrity — conditions such as atopic dermatitis, eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease (keratosis follicularis). **Pregnancy** • Animal reproduction studies have not been conducted with VIGIV; therefore, it is not known whether VIGIV can cause fetal harm when administered during pregnancy or whether it can affect reproductive capabilities. • However, immune globulins have been widely used during pregnancy for many years without any apparent negative reproductive effects. The risk/benefit of VIGIV administration should be assessed for each individual case. • The decision to treat should involve Maternal- Fetal medicine consultation. • Pregnant women with severe mpox infection (and, given expected severity, this includes suspected clade I cases) or complex obstetric conditions should be admitted to hospital - this is a tertiary hospital or designated centre (e.g. Mater/ CUMH). • **Lactation** • It is not known whether VIGIV is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VIGIV is administered to a woman who is nursing.

Paediatric & Geriatric considerations	• Safety and effectiveness in the paediatric population (< 16 years of age) and geriatric population (> 65 years of age) have not been established for VIGIV. • All children with mpox infection should be discussed with the Paediatric Infectious Disease service in Children's Health Ireland.
Formulation	• VIGIV contains human *vaccinia virus* immune globulin and inactive ingredients, maltose and polysorbate 80. VIGIV is a preservative-free injection product that is supplied in a 20 mL single dose vial containing ≥ 50,000 Units per vial of neutralizing vaccinia immune globulin antibodies. 20 mL refers to the vial size, not the fill volume, which varies by lot (~ 8-12 mL/vial). Each VIGIV vial is filled to contain ≥ 50,000 Units regardless of the fill volume. The exact volume or concentration (Units/mL) is NOT indicated on the vial label itself. VIGIV does not contain natural rubber latex. • VIGIV is kept frozen at/below ≤ -15°C (≤ 5°F) for long-term storage in the SNS. The product may be shipped from SNS refrigerated at 2°C to 8°C (36°F to 46°F). Once thawed, VIGIV should be used within 60 days of thawing when kept refrigerated at 2°C to 8°C (36°F to 46°F). Do NOT refreeze. Do not use after the expiration date. All vials must remain upright protected from light. If the product is received frozen at/below 15°C5 (≤5°F), VIGIV vials may be maintained frozen by placing into freezer ≤ 5°F (≤ -15°C) at the hospital/facility, which provides longer expiry. Otherwise, store refrigerated at 2°C to 8°C (36°F to 46°F) and use within 60 days of thawing. • Intravenous infusion should begin within 4 hours after puncturing the vial. Do not save punctured VIGIV vials for future use since it contains no preservatives. Discard partially used vials.
Route of administration	VIGIV is for intravenous use only.
Dose and duration of therapy	VIGIV dose is based on actual body weight: 6,000 U/kg is administered as soon as symptoms appear and are judged to be due to OPXV infections or severe vaccinia virus vaccination complications. Higher, initial dose (e.g., 9,000 U/kg) may be considered for patients with severe disease based on clinical judgment. Higher doses (e.g., 9,000 Units/kg, 24,000 Units/kg) may be considered in the event that the patient does not respond to the initial 6,000 or 9,000 U/kg dose. In clinical trials, administration of higher doses of up to 24,000 Units/kg was shown to be safe and well tolerated and to decrease the endogenous immune response to vaccinia vaccine along with a concomitant decrease in vaccination lesions.

Method of administration	Instructions on How to Calculate the Weight-Based VIGIV Dose by Units and Corresponding Volume for Dosing Preparation can be found **here**. **Patients with Renal Insufficiency** Use VIGIV with caution in patients with pre-existing renal insufficiency and in patients at increased risk of developing renal insufficiency. Monitor renal function and urine output in patients at risk of renal failure. Check baseline blood viscosity in patients at risk of hyper viscosity and conduct confirmatory tests if haemolysis or transfusion-related acute lung injury (TRALI) is suspected. • VIGIV is for intravenous use only. • VIGIV dose is based on actual body weight: 6,000 Units/kg is administered as soon as symptoms appear and are judged to be due to OPXV infections or severe vaccinia virus vaccination complications. Higher, initial dose (e.g., 9,000 Units/kg) may be considered for patients with severe disease based on clinical judgment. • Since efficacy of live attenuated virus vaccines (e.g., measles, rubella, mumps, and varicella) may be impaired by immune globulin administration, revaccination may be necessary. Vaccination with live virus vaccines should be deferred until approximately three months after administration of VIGIV. Persons who receive VIGIV shortly after live virus vaccination should be revaccinated 3 months after the administration of the immune globulin.
Drug-drug interactions	• JYNNEOS is a live, replication-deficient vaccinia virus vaccine for prevention of mpox and smallpox. Since VIGIV contains antibodies to OPXVs, VIGIV could interfere with desired immunogenicity to JYNNEOS if it is administered in close temporal proximity to VIGIV. It is ideal to delay administration of JYNNEOS if VIGIV was recently administered. During outbreaks or depending on specific individual cases, however, administering a dose of JYNNEOS after VIGIV administration without delay may be appropriate. Case specific consultation with the CDC poxvirus clinical team is available. • Admixtures or VIGIV with other drugs have not been evaluated. It is recommended that VIGIV be administered separately from other drugs that the patient may be receiving. If a pre-existing catheter must be used, the line should be flushed with 0.9% Sodium Chloride and not with other solutions such as dextrose in water.
Adverse effects	• The adverse drug reactions to VIGIV treatment in clinical trials (>10%) include headache, nausea, rigors, and dizziness. Other adverse events associated with infusion of immunoglobulins include hypotension, pallor, diarrhoea, joint pain, dizziness, hyperkinesis, drowsiness, pruritis, rash, renal dysfunction, perspiration, and vasodilation.

	• Although there were no serious adverse drug reactions reported following administration of VIGIV in clinical trials, there has been a post-marketing case of severe vaccinia infection that developed intravascular haemolysis, leukopenia, and thrombocytopenia during VIGIV treatment.

1.5.5 Vaccination

Vaccination campaigns were implemented in the EU/EEA and other countries to control the outbreak of clade IIb MPXV in 2022, with a third-generation non-replicating smallpox vaccine authorised by the European Medicines Agency (EMA) for protection against mpox in individuals aged 18 years and above.

In the present epidemiological situation, mass vaccination and general travel vaccination in the Ireland is not required; current vaccination approaches should follow an 'at risk' principle:

- Primary preventative (pre-exposure) vaccination (PPV);
- Post-exposure preventative vaccination;[2] and
- Vaccination to certain individuals at high risk.

The most current vaccine guidance can be found **here** (mpox chapter). [23]

1.5.6 Public Health Management

1.5.6.1 Contact Tracing

H&CWs and non-H&CWs management based on exposure risk can be found in Chapter 4.

The related monitoring forms based on exposure risks are available **here**.

1.5.6.2 Reporting Requirements

Clinicians and laboratories are **legally required to report certain infectious diseases** to the Medical Officer of Health of their regional Department of Public Health. In Ireland, the HPSC has been encouraged to ensure that clade and subclade determination reporting of cases is possible on the national reporting system, this approach will allow for more granular insight into the epidemiology of mpox.

Enhanced surveillance forms and related protocols are in place to ensure effective delivery of contact tracing services and surveillance requirements. The regional Department of Public Health where the case resides will remain involved in the investigation of non-sexual contacts. The regional Department of Public Health will also remain available to advise Sexual Health Service (SHS) on the public health management of contacts of high complexity, as required. Some of these may arise and are listed above (*NB: this list is not exhaustive*).

[2] Pending clarification around funding for post-exposure prophylaxis vaccination administration by Sexual Health Services for sexual contacts on mpox cases, review on case-by-case basis will need to be considered with Departments of Public Health and local Sexual Health Services.

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3 Additional Resources

- Clinical Treatment of Mpox | Mpox | CDC
  Development of CMX001 for the Treatment of Poxvirus Infections
  https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214460s000,214461s000lbl.pdf

- https://www.ijidonline.com/article/S1201-9712(06)00040-3/fulltext

- Community spread of a human monkeypox virus variant with a tecovirimat resistance-associated mutation | Antimicrobial Agents and Chemotherapy

- https://www.unboundmedicine.com/ucentral/view/Johns_Hopkins_ABX_Guide/540718/all/Tecovirimat?q=tecovirimat

4 APPENDIX A

4.1 Contact details for relevant health services and laboratories.

Clinics that provide mpox testing and times

- Further information on HSE STI Services in Ireland can be found **here.**

Laboratories that provide mpox testing and times

- UCD National Virus Reference Laboratory User Manual and Pathogen Index can be found **here**.

5 APPENDIX B

5.1 Additional resources for healthcare providers and patients.

Contact Details for Public Health in each HSE Health Region

- Contact details for each regional Department of Public Health can be found **here**.

Resources for patients:

- Information for people with confirmed/suspected mpox can be found **here**.

6 APPENDIX C

6.1 Summary of Therapeutic Options

SUMMARISED MECHANISMS of ACTION, ADMINSTRATION RECOMMENDATIONS, ADVERSE EVENTS, CLINICAL CONSIDERATIONS, and SUPPORTING DATA ABOUT MEDICAL COUNTERMEASURES THAT CAN be USED to TREAT MPOX

CONSIDERATIONS	MEDICAL COUNTERMEASURES	
	Tecovirimat (Tpoxx or ST-246)	Immunoglobulin
Description	An OPXV-specific antiviral with limited activity against unrelated RNA or DNA viruses	Solvent- or detergent-treated, filtered sterile solution of purified immune globulin from human plasma of persons with antibodies to vaccinia virus.
Mechanism of action against OPXVs	Inhibits association of VP37 (a protein encoded by and highly conserved across the OPXV genus) with a cellular protein, preventing formation of egress-competent envelope virions necessary for cell-to-cell dissemination of virus	Provides passive antibody which might have cross-reactivity across the OPXV genus .
Dose	200-600 mg depending on weight[A]	6,000–9,000 units/kg[B]
Route	Oral (capsules)	IV
Frequency	Every 8 to 12 hours depending on weight	Single dose but can be repeated depending on duration of illness and severity of immunocompromise
Duration	14 days unless indication to prolong[C]	NA
Potential adverse events	Dizziness, headache, nausea, diarrhoea, itching, and abdominal pain.	Adverse events associated with infusion of immunoglobulins (e.g., headache, diaphoresis, erythema, anaphylaxis, thrombosis, acute kidney injury, and volume overload).
Warnings		Other warnings: Hypersensitivity, renal dysfunction, interference with blood glucose testing, thrombotic events, aseptic meningitis syndrome, haemolysis, transfusion-related acute lung injury, and transmission of infectious agents from human plasma.
Drug interactions	Might reduce levels of NNRTI rilpivirine. Might increase concentration of blood glucose-lowering agent repaglinide causing hypoglycaemia. Decrease concentration of midazolam .	Vaccination with live virus vaccines (e.g., varicella, measles, mumps, and rubella) should be deferred for 3 months after use.
Data from selected animal studies	Cynomolgus macaques were lethally challenged IV with MPXV and treated on day 4, 5, and 6 post challenge. Treatment with tecovirimat for 14 days resulted in statistically significant improvement in survival relative to placebo, except when given starting at day 6 post challenge.	In a mouse-tail lesion model, VIGIV exerted a protective effect against vaccinia infection when compared with a negative control.

Data from use in humans	Of 255 patients treated during the outbreak,[D] the median interval to first subjective improvement was 3 days with limited adverse events reported.	Evidence for smallpox prevention when given to high-risk contacts Mixed evidence for efficacy for treatment of progressive vaccinia.
Pregnancy, breastfeeding, and fertility considerations	Likely safe in pregnancy and breastfeeding without affecting fertility.	Likely safe in pregnancy and breastfeeding without affecting fertility.
CNS considerations	Penetrates well.	Penetrates to limited degree.
Resistance considerations	Single point mutation can confer resistance.[E]	NA
Miscellaneous considerations	High-fat (approximately 600 calories and 25g fat) meal required with each oral dose.	Vaccinia-specific antibody, which might cross-react with MPXV. Might interfere with endogenous antibody production and IgG antibody testing. When used to treat vaccinia keratitis in rabbits, VIGIV resulted in prolonged scarring and stromal oedema.

Footnotes:

A: See section 1.5.4.2 Alternative Therapeutics for weight specific dosing.

B: Data suggest that an aggressive early dosing regimen for patients with severe immunocompromise might be most beneficial; for this reason, a dose in the higher range (9,000 units/kg) early in the clinical course, potentially followed by an additional dose 3–4 days later, might help saturate viral antigens and halt viremia and viral replication.

C: The standard duration of tecovirimat treatment is 14 days, with clinical data being limited to a 14-day course. Based on individual patient risk-benefit assessment and disease progression, tecovirimat may be extended beyond 14 days, or shortened because of lack of virologic or clinical response or adverse event occurrence.

D: **https://www.cdc.gov/mmwr/volumes/71/wr/mm7137e1.htm?s_cid=mm7137e1_w**

E: During 2023, <0.5% specimens (out of >5,000 specimens) sent to CDC for testing have been found to develop resistance.