Clinical Commissioning Rapid Policy Statement:

Tecovirimat as treatment for patients hospitalised due to monkeypox virus infection

Publication date: 20 September 2022

Commissioning position

Tecovirimat is recommended to be available as a treatment option for patients hospitalised due to monkeypox virus infection within the criteria set out in this document.

Background

Tecovirimat is a novel antiviral developed and manufactured by SIGA Technologies. Tecovirimat inhibits the viral envelope protein p37. This protein is present and highly conserved (approximately 98% amino acid identity) in all orthopoxviruses. Inhibition of p37 prevents the formation and egress of enveloped virions, which are essential for orthopoxvirus virulence.

Tecovirimat was granted authorisation under ‘exceptional circumstances’ by the Medicines and Healthcare products Regulatory Agency (MHRA) on 30 June 2022 for use in England, Scotland and Wales and authorised by the European Medicines Agency (covering its use in Northern Ireland) on 6 January 2022 under ‘exceptional circumstances’ for the treatment of monkeypox (as well as smallpox and cowpox) in adults and children with a weight of at least 13kg.

There is currently no published human trial data to support the use of tecovirimat for the treatment of monkeypox. A randomised trial in non-hospitalised patients is ongoing (PLATINUM). Studies have reported improved survival from lethal monkeypox virus infections in tecovirimat-treated animals compared to placebo-treated animals at different stages of disease (Quenelle DC et al, 2007) (Grosenbach DW et al, 2018). The safety of tecovirimat has been evaluated in a study of 359 human volunteers in which the frequency and severity of adverse events was largely similar in the tecovirimat and placebo groups (Grosenbach DW et al, 2018). To date, there is published data on a single patient with monkeypox infection treated with tecovirimat (Adler H et al 2022). In this patient, tecovirimat was well tolerated and rapid viral clearance was observed after treatment initiation. The World Health Organization states: that if tecovirimat is used for patient care, it should ideally be monitored in a clinical research context with prospective data collection Monkeypox (who.int).

This rapid policy statement outlines the eligibility criteria for the use of tecovirimat in the treatment of hospitalised patients with monkeypox virus infection. The use of tecovirimat as described in this policy is unlicenced because the medicine is currently imported US-labelled stock.

Eligibility criteria

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

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

AND

- symptomatic with a syndrome compatible with ongoing monkeypox virus infection

AND

- meeting any one or more of the criteria[1] for severe or complicated disease as outlined below:
    - critical illness where monkeypox virus infection is considered to be a key factor driving the critical condition of the patient
    - intractable pain
    - 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 Green Book definitions
    - ocular or periocular disease
    - encephalitis, meningitis or other neurological manifestation
    - extensive cutaneous disease (for example more than 100 lesions)
    - complex genital disease: difficulty passing urine due to swelling or lesions causing direct urinary obstruction

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
- Adults and children of less than 13 kg body weight

[1] By exception, treatment outside the above “severe” criteria may be used in the context of treating children or to facilitate shortening the duration of infectiousness due to other complex medical needs. Such treatment must be considered and agreed by the appropriate multidisciplinary team.

Dose

The recommended dose of tecovirimat in adults and children weighing 13 kg and above is listed below:

Body Weight	Dosage	Number of Capsules
13 kg to less than 25 kg	200 mg every 12 hours for 14 days	One tecovirimat 200mg capsule
25 kg to less than 40 kg	400 mg every 12 hours for 14 days	Two tecovirimat 200mg capsules
40 kg and above	600 mg every 12 hours for 14 days	Three tecovirimat 200mg capsules

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

Cautions

Please refer to the Summary of Product Characteristics (SmPC) for tecovirimat for special warnings, precautions for use and interactions with other medicinal products.

- Severe renal impairment (please see the SmPC)
- Severe hepatic impairment (please see the SmPC)
- Pregnancy
- Breastfeeding

The SmPC for tecovirimat currently states that: “There are no data from the use of tecovirimat in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). 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.

For women who are breast-feeding, the SmPC for tecovirimat states: “It is unknown whether tecovirimat/metabolites are excreted in human milk. Available toxicological/safety data in animals have shown excretion of tecovirimat in milk (see section 5.3). A risk to the newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with tecovirimat.”

Marketing authorisation

Tecovirimat SIGA 200 mg hard capsules are licensed in Great Britain and Europe. The tecovirimat 200 mg capsules (TPOXX) to be supplied in the UK for use under this clinical policy are initially from US emergency use stock and should be considered an unlicensed product within the UK. The FDA product labelling is available.

The MHRA-approved product information (Summary of Product Characteristics (SPC) and

Patient Information Leaflet (PIL) is available on the MHRA website. The EMA-approved product information (Summary of Product Characteristics (SPC)) can be found on the EMA website.

Governance arrangements

Use of unlicensed medication

Any provider organisation treating patients with unlicensed products will be required to assure itself that the internal governance arrangements have been completed before the medicine is prescribed. These arrangements may be through the health board/hospital/trust's drugs and therapeutics committee, or equivalent.

Provider organisations in England should register all patients using prior approval software (alternative arrangements in Scotland, Wales and Northern Ireland will be communicated) and ensure monitoring arrangements are in place to demonstrate compliance against the criteria as outlined.

Clinicians are also required to ensure that any data collection requirements are met for the purpose of ongoing surveillance, audit and relevant evaluation, including of clinical effectiveness, around the use of tecovirimat (see 'Surveillance, service evaluation and research' section below).

Surveillance, service evaluation and research

There is an urgent need to generate more evidence and develop greater understanding around the use of tecovirimat in the treatment of patients with monkeypox infection. Both surveillance and service evaluation are necessary to gain knowledge around the following:

- factors of relevance in determining monkeypox treatment;
- the impact of tecovirimat in hospital settings on the immune/virologic response and clinical recovery; and
- the public health sequelae of tecovirimat use, such as generation of new mutations and/or variants

Treating clinicians are asked to ensure that all PCR tests undertaken as part of routine clinical care are processed via the hospital laboratory where these samples should be retained for sequencing. Further serial sampling for specific patient groups may be requested as part of UKHSA genomic surveillance purposes, or country specific programmes.

Clinicians must ensure that any additional data collection requirements are met for the purpose of relevant surveillance, audit and evaluation around the use of tecovirimat. It is expected that there will be ongoing monitoring (involving sample collection) of selected patients treated with tecovirimat (led by UKHSA, for instance around the potential generation of new variants), as well as academic research to generate new knowledge around clinical effectiveness and other relevant aspects of public health.

In addition to public health-based surveillance there will be opportunities to participate in clinical research studies. Clinicians should actively support recruitment of patients with laboratory confirmed monkeypox infection and with active skin or mucosal lesions, but who do not require hospital admission, to the PLATINUM trial. An observational study, MOSAIC, exploring outcomes of patients with monkeypox infection across Europe is also currently underway (MOSAIC).

Policy review date

This is an interim rapid clinical policy statement, which means that the full process of policy production has been abridged: public consultation has not been undertaken. This policy may need amendment and updating if, for instance, new trial data emerges, supply of the drug changes, or a new evidence review is required. A NICE Technology Appraisal or Scottish Medicines Consortium (SMC) Health Technology Assessment or All Wales Medicines Strategy Group (AWMSG) appraisal of tecovirimat for monkeypox virus infection would supersede this policy when completed.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment, and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Intractable pain	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)

References

Quenelle, DC., et al. (2007) 'Efficacy of delayed treatment with ST-246 given orally against systemic orthopoxvirus infections in mice', *Antimicrobial Agents and Chemotherapy,* 51, pp.689-95.

Grosenbach, D.W., et al. (2018) 'Oral tecovirimat for the treatment of smallpox', *New England Journal of Medicine*, *379*(1), pp.44-53.

Adler, H., et al. (2022) 'Clinical features and management of human monkeypox: a retrospective observational study in the UK', *The Lancet Infectious Diseases,* 22, pp 1153-1162.