

High Consequences Infection Disease Network	Pharmacy Information
Drug	Tecovirimat - ORAL
Version	V10 26/9/22 – NCL specific update
Review	Review in 1 year (or soon as emerging data becomes available)
Author:	Lead Pharmacists from the following UK HCID Centres: <ul style="list-style-type: none"> • Guy's and St Thomas' NHS Foundation Trust • Royal Free London NHS Foundation Trust, • Imperial College Healthcare NHS Foundation Trust • Royal Liverpool and Broadgreen University Hospitals NHS Trust • Sheffield Teaching Hospitals NHS Foundation Trust

Disclaimer: This document is designed to be used as summary pharmacy guidance around oral tecovirimat. We will endeavour to ensure that this is updated as soon as new information comes to light.

Indication	<p>The drug is licensed within the EU but not the UK. Hospitals using tecovirimat are required to follow their own internal governance processes for approval of unlicensed medicines.</p> <p>Licensed for the treatment of the following viral infections in adults and children with body weight at least 13 kg:</p> <p>Smallpox Monkeypox Cowpox</p> <p>Tecovirimat is also indicated to treat complications due to replication of vaccinia virus following vaccination against smallpox in adults and children with body weight at least 13 kg</p> <p>Tecovirimat should only be commenced on the advice of HCID Network discussion.</p>																							
Presentation	<p>200mg capsules supplied in packs of 42. This is enough for a week at a standard adult dose of 600mg twice a day.</p> <p>The IV formulation has recently been licensed within the USA but currently this is not available within the EU/UK</p>																							
Mechanism of action	<p>Interfering with a protein called VP37 that is found on the surface of orthopoxviruses, including smallpox, monkeypox and cowpox. By interacting with this protein, the medicine prevents the viruses from reproducing normally, slowing down the spread of infection.</p>																							
Dosing	<table border="1"> <thead> <tr> <th>Body Weight</th> <th>Dosage</th> <th>Number of Capsules</th> </tr> </thead> <tbody> <tr> <td>Greater than 120kg</td> <td>600mg every 8 hours for 14 days</td> <td>3 x 200mg thrice a day</td> </tr> <tr> <td>40kg to 120kg</td> <td>600mg every 12 hours for 14 days</td> <td>3 x 200mg twice a day</td> </tr> <tr> <td>25kg to less than 40kg</td> <td>400mg every 12 hours for 14 days</td> <td>2 x 200mg twice a day</td> </tr> <tr> <td>13kg to less than 25kg</td> <td>200mg every 12 hours for 14 days</td> <td>1 x 200mg twice a day</td> </tr> <tr> <td>6kg to less than 13kg (off-label use)*</td> <td>100mg every 12 hours for 14 days</td> <td>See special instructions</td> </tr> <tr> <td>Less than 6kg (off-label use)*</td> <td>50mg every 12 hours for 14 days</td> <td>See special instructions</td> </tr> </tbody> </table> <p>*Currently, the NHSE commissioning policy excludes adults and children <13kg body weight. Data under 13kg is based on PKPD modelling from the manufacturer (SIGA).</p>			Body Weight	Dosage	Number of Capsules	Greater than 120kg	600mg every 8 hours for 14 days	3 x 200mg thrice a day	40kg to 120kg	600mg every 12 hours for 14 days	3 x 200mg twice a day	25kg to less than 40kg	400mg every 12 hours for 14 days	2 x 200mg twice a day	13kg to less than 25kg	200mg every 12 hours for 14 days	1 x 200mg twice a day	6kg to less than 13kg (off-label use)*	100mg every 12 hours for 14 days	See special instructions	Less than 6kg (off-label use)*	50mg every 12 hours for 14 days	See special instructions
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Special Instructions	<p>Tecovirimat should be administered within 30 minutes following a meal/feed of moderate to high fat content (600 calories and ~25 grams of fat to ensure that a substantial meal or food given).</p> <p>Tecovirimat has a relatively low resistance barrier therefore, patients should be counselled on the</p>																							

	<p>importance of adherence to the full 14-day treatment and taking with a high fat meal.</p> <p>For doses < 200mg: Company data suggests that they were unable to obtain consistent suspension in either milk or baby formula with the two lowest doses. Thus, administration is recommended via nasogastric tube where available.</p> <p>If production facilities are available, unit-dose powders may be weighed out and dispensed as per local procedure. This gives an accurate measure of the drug powder.</p> <p>The 200mg Tecovirimat capsules contain: 390 mg of powder of which 200 mg is tecovirimat.</p> <p>Note: Tecovirimat monohydrate exhibits low solubility in water and buffers of the gastrointestinal pH range. If dispersing capsule contents in a fixed volume of water for a proportional dose, the accuracy and consistency of the dose cannot be guaranteed.</p> <p>The dose can be mixed with feed as long as the whole feed is administered.</p> <p>The entire mixture should be administered within 30 minutes of preparation</p> <p>Experience with infants from Imperial College Healthcare NHS Trust Paediatric HCID is to open the capsule and mix the Tecovirimat powder with 30ml of water. Then take the fraction required for the dose.</p>
Elderly / Renal / Hepatic	<p>No dosage adjustments are required.</p> <p>To the best of our knowledge no dose adjustment is required on renal replacement therapy</p>
Therapeutic Drug Monitoring	<p>Therapeutic Drug monitoring may be able to be carried out but only after discussion with the company, your local laboratory and if there is clinical need. Contact SIGA directly via: monkeypox@sig.com together with HCID pharmacists from Royal Free, Imperial, GSTT for pragmatic advice.</p>
Pregnancy / breastfeeding	<p>Use in this context requires a risk/benefit discussion. The SPC states that use in either pregnancy or breast-feeding is not recommended</p> <p>Pregnancy: No human data. No embryofetal developmental toxicity was noted in mice models at supra-therapeutic doses than the equivalent human recommended dose.</p> <p>Breastfeeding: No human data. Data suggests drug is excreted in milk. As per pregnancy data. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for tecovirimat.</p>
Interactions	<p>The SPC above is relatively extensive. Tecovirimat SIGA, tecovirimat monohydrate (europa.eu)</p> <p>UpToDate has some further information. Tecovirimat (United States: Availability limited to strategic national stockpile distribution): Drug information - UpToDate</p> <p>University of Liverpool drug interactions checker – Liverpool HIV Interactions (hiv-druginteractions.org) for review of interaction between antiretrovirals and tecovirimat only. Tecovirimat can be selected as a co-medication and interactions will only be checked between HIV drugs entered and tecovirimat and not between Tecovirimat and other co-medications entered.</p>
Side effects	<p>The most common side effects with Tecovirimat are headache (which may affect more than 1 in 10 people) and nausea (which may affect up to 1 in 10 people)</p>
Storage	<p>Store below 25°C and in the original package in order to protect from light.</p> <p>If patient to be discharged home with supply of medication then ensure stored in light protective container if not kept in original package.</p>
Prescribing criteria for use & BlueTeq requirements	<ol style="list-style-type: none"> 1. Confirm that patient meets the criteria set out in the Clinical Commissioning Rapid Policy Statement: Tecovirimat as treatment for patients hospitalised due to monkeypox virus infection https://www.cas.mhra.gov.uk/ViewAndAcknowledgment/viewAlert.aspx?AlertID=103213 2. If patient is < 13kg or pregnant contact your local specialised infectious diseases centre for further advice. All cases for paediatrics/ maternity cases should be discussed with

	<p>Paeds ID Centres for cascade to national call.</p> <ol style="list-style-type: none"> 3. Ensure the Trust’s clinical governance measures have been followed and the medication is approved for use within the organisation e.g. application to Drugs and Therapeutics Committee [Chair’s action when urgent clinical need] 4. Add the medication to the Trust pharmacy and prescribing systems, if not already present 5. Ensure the Trust has registered for using tecovirimat via the BlueTeq system via SITE registration form. This may take 24 hours to appear. Complete a patient form for each patient that requires tecovirimat once site approved. 6. Confirm the appropriate distribution route depending on clinical urgency
Requesting supply	<p>Supply is considered clinically urgent if:</p> <ul style="list-style-type: none"> • Critical illness where monkeypox virus infection is considered to be a key factor driving the critical condition of the patient (<i>defined as requiring admission to level 2 or 3 environment</i>) or • Ocular or periocular disease or • Encephalitis, meningitis or other neurological manifestation* • Upper respiratory tract mucocutaneous involvement that is affecting swallowing or airways <ol style="list-style-type: none"> 1. Identify the distribution site nearest to the Trust. In NCL, Royal Free London is a ‘distribution site’ and can field requests from other NCL Trusts for stock. UCLH are a ‘holding’ site (hold stock for internal use only). 2. Arrange a purchase order and contact the distribution site to arrange delivery to the appropriate location 3. Requesting site will need to arrange the courier transfer and ensure that there is someone available at the requesting site who can receive supply when it arrives
References	<ol style="list-style-type: none"> 1. Tecovirimat SIGA, tecovirimat monohydrate (europa.eu) (accessed June 2022) 2. SIGA Pharmaceuticals – personal correspondence re: < 13kg dosing & TDM Process. 3. SIGA Pharmaceutical Investigatory Brochure re: Pregnancy & Breastfeeding 4. Dosing >120kg Tecovirimat (United States: Availability limited to strategic national stockpile distribution): Drug information - UpToDate 5. https://www.cas.mhra.gov.uk/ViewAndAcknowledgment/viewAlert.aspx?AlertID=103213

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